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ORIGINAL LECTURES.

CARTWRIGHT LECTURES.

ON CERTAIN PROBLEMS IN THE PHYSIOLOGY OF THE BLOOD CORPUSCLES.

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BY WILLIAM OSLER, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA.

LECTURE I.

THE BLOOD PLAQUE.

Introduction.—Around the blood corpuscles still centre some of the most interesting questions in physiology and pathology, and though amid microbes and cultures we may have forgotten them for the moment, they are nevertheless still calling for solution, and perplexing this quite as much as any of the six or seven generations which have passed away since Loeuwenhoek first detected the red corpuscles in the human blood.

The origin and life history of the corpuscles of the blood have been, and still are, among the great secrets of physiology. Strange, indeed, is it to think of the thousands of able observers who have gazed long and ardently, with rude and with perfect instruments, vainly endeavoring to solve the riddle constantly propounded by these common objects of study. In no department of physiology has so much labor been spent with so little apparent result. While in other lines we have penetrated to the centre of certain biological mysteries, the progress here seems painfully slow, and the discovery by Wharton Jones, in 1846, of the amœboid power of the colorless corpuscles, the rediscovery by Cohnheim of their migratory power, and the discovery of the blood-forming function of the marrow, may be said to be the most important additions to our knowledge in this generation.

The activity of research during the past decade has had, however, a perceptible influence, and there are signs of breaking in the heavy clouds which overhang the origin of these corpuscles, and the darkness is certainly less dense than it was.

A peculiarity of these perennial problems is that certain phases for the time engage the attention of observers, and the laboratory activity the world over seems centred upon them, with the result, in a few years, of an enormous increase in the literature, and after the question has been thoroughly fought out and quiet is resumed, we are thankful if only an outpost has been gained in the struggle and we are a step nearer to the citadel of truth.

As regards the blood corpuscles, the work of the past few years has been largely in two directions—toward the determination of the existence or non-existence of a third corpuscle in the blood, and in the study of the histological processes attending degeneration and regeneration of the corpuscles in disease, and upon these subjects I shall hope to engage your attention during this course.

I propose, therefore, in the first lecture to consider the much debated third corpuscle, or hæmatoblast of Hayem, which, so far as I know, has not yet received systematic consideration before any American or English audience. In the second I shall discuss certain histological problems connected with the degeneration and regeneration of the blood corpuscles; and in the third I shall present a statement of recent views on the relation of the corpuscles to coagulation.

THE THIRD CORPUSCLE OR BLOOD PLAQUE.

Definition.—A colorless protoplasmic disk, constant in mammalian blood, measuring from 1.5 to 3.5 micromillimetres. The number per cubic millimetre in the blood of a healthy adult is about 250,000, but their number varies greatly at different periods of life and with varying conditions of health and disease. The ratio to the red is about 1 to 18 or 20. They are delicate elements, and, like the red corpuscles, tend on the withdrawal of the blood to adhere to one another, when they form the irregular granular clumps which have long been known as Schultze's granule masses.

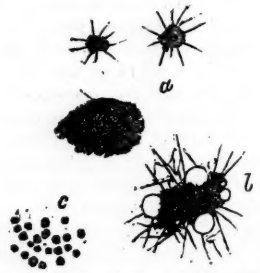
Name.—It will be necessary, at the outset, to refer to the names which observers have given to this corpuscle. Unfortunately they are rather numerous, and no one of them entirely satisfactory. Donné,[1] whose description is the earliest, called them *globulins*. Zimmerman[1] spoke of them as *elementary corpuscles*. Later, the collected groups were referred to as "*granular débris*" or Schultze's[3] *granule masses*. Among the more recent observers, Hayem[4] gave the name of *hæmatoblasts*, and Bizzozero[5] that of *blutplattchen—blood-plate*. Various writers refer to this element as the *third corpuscle*, while in the research of Kemp,[6] just issued from the Biological Laboratory of Johns Hopkins University, the term *plaque* is used and has received the sanction of Prof. Martin. To the terms *third corpuscle* and *hæmatoblast* there is the serious objection that these names have been applied to other bodies which have nothing to do with the elements in question. The former, to the so-called invisible corpuscle[1] of Norris, and the latter to the nucleated red corpuscle of the bone marrow. The name hæmatoblast, moreover, carries with it certain theoretical conceptions regarding the functions of these bodies which may or may not be true. I am inclined to favor the name which Bizzozero has adopted, partly

[1] Shortly after the publication of Bizzozero's paper, Norris claimed that the corpuscles described in it were the same as the barely visible corpuscles of his "fugitive group," but a study of the beautiful photographs in his book, will, I think, convince anyone with a practical knowledge of the blood-plates of Bizzozero, that they are separate elements. The granules which he figures (Fig. 45) as resulting from the breaking up of the younger or fugitive corpuscles are in reality the disintegrated blood-plates. Moreover, the corpuscles which he figures are uniformly larger than the blood-plates.

because we are indebted to the distinguished Turin Professor for a series of able researches which have awakened the liveliest interest in these corpuscles, and partly because usage of late has confirmed the name. Blood-plate, the English equivalent of the word *blutplattchen*, is by no means euphonious, while the French *plaque*, adopted by Kemp, is perhaps more convenient and might be employed in the future by American and English writers.[1]

Methods of Study.—Let us first consider the plaques in blood examined in the usual manner, without the addition of any reagent; and let us suppose the blood to be taken from a case of consumption or cancer, or from a newborn animal, as in these states these corpuscles are abundant. We then find, in addition to the red and colorless corpuscles, many grayish-white granular masses of various sizes and shapes. Examined at once, and if too much pressure is not exercised by the top-cover, the edges of these masses are clearly defined and they form compact aggregations. With a power of 500 diameters, the composite structure is well seen and the granular character is plainly discernible to be due to

FIG. 1.



a. Aggregations of plaques in human blood, forming the so-called *granule masses* of Max Schultze. *b.* Disintegration of the plaques, with fibrin filaments and mucin-like spheres adhering to the mass. *c.* Isolated plaques.

the agglutination of numerous small bodies of uniform size. At the edges, isolated or partially free corpuscles can usually be noticed. The fibrin filaments, as coagulation proceeds, seem to radiate from the masses as centres. This remarkable conglutination of the plaques and a tendency to undergo rapid change have retarded greatly the recognition of the corpuscles as veritable elements of the blood. Observers have, as a rule, seen in them nothing more than a granular débris of no special significance. Nor is this to be wondered at, as they so quickly undergo change that the clusters, in the course of a short time, really present the appearance of disintegrating protoplasm (Fig. 1, *b*). The size and shape of the groups are most variable; the more abundant, as a rule, the plaques the larger and more numerous the aggregations; the smaller ones, composed of two or three plaques, may not equal in size a red corpuscle, while the larger ones may be ten or fifteen times this size. A tendency to adhere to foreign particles is very noticeable, and they will collect in numbers upon a fine thread of cotton or linen. In the normal blood of the adult the plaques are not very numerous, and so do not form very large collections. In some individuals, however, in health the groups are always of considerable size. There are conditions of the blood in which, from some cause, the attraction of the plaques to each other appears diminished, and instead of forming large masses, they adhere to the slide either isolated or in scattered groups of from two to ten in number (Fig. 1, *c*). Possibly this may be an accident of preparation, but I am inclined to think it not, from the fact that I have noted it in cases of malignant fever, smallpox, scarlet fever,—the very states in which the normal process of nummulation of the red corpuscles may be so altered that the cells aggregate into compact clumps. In fact, the red corpuscles and the plaques in normal blood have each their peculiar mode of aggregation, the red in series and the plaque in masses. I have never seen any appearance which would suggest that the plaques have the slightest tendency to adhere by their flat surface, and to form rouleaux, as the red. It will be found too, I think, that just as there are, apart from modes of preparation, peculiarities which interfere with the normal nummulation of the red, so there are conditions in which the plaques present variations in their usual method of aggregation.

It was a consideration of the relative size of the masses, and the impossibility of their passing through the capillaries, which led me in 1873, in University College Laboratory, London, to the discovery of their corpuscular nature; and it was found that while in the blood of the young rat, when withdrawn, the masses were numerous and large, in the bloodvessels the collections, as such, never occurred, but innumerable small corpuscles, similar in character to those seen at times so plainly at the edge of the masses.

To study the plaques properly, the blood must be allowed to pass directly into a solution which, while preventing conglutination, does not materially alter their form or characters. Or they may be, perhaps, more satisfactorily observed while still within the bloodvessels.

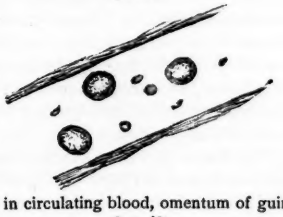
Various solutions have been employed by different observers. Zimmerman, whose study of these corpuscles was really very complete, allowed the blood to flow directly into a solution of a neutral salt which prevented coagulation, and then in the supernatant fluid he found small colorless cells in extraordinary numbers. I have repeatedly confirmed this observation in the case of horses' blood, when demonstrating the common experiment of preventing clotting, by letting the blood flow into sodium sulphate. The plaques abound in the clear serum, and if the solution is not too concentrated they are very little altered. In using the hæmatocytometer (Gowers), the sulphate of soda with which the blood is mixed acts in the same way, although in the counter it is more common to find the plaques aggregated than isolated, but the individual plaques are unusually distinct. More suitable solutions for histological purposes are osmic acid 1 per cent., the fluids of Pacini, modified by Hayem, and of Bizzozero. Pacini's solution, as used by Hayem, consists of sodium chloride 1 part, sodium sulphate 5 parts, corrosive sublimate 0.5 part, in 200 of distilled water. Bizzozero employs the ordinary salt solution, ¾ per cent., to which methyl-violet has been added. Afa-

[1] I did think of suggesting the word *disklet* as very suitable for these *little disks*, but I had not the courage to add another to the already long list; moreover, as my own name has been used in connection with these bodies, I felt absolved from further sponsorial duties on their behalf.

nassiew[10] recommends strongly the use of salt solution to which 0.5 per cent. of dried pepsin has been added, and 1 to 1000 of methyl-violet, and a small amount of sublimate or carbolic acid to prevent decomposition. I find that the Pacini fluid and osmic acid answer every purpose, and in them the plaques undergo very little change. The examination is made in the following way: Upon the thoroughly cleansed finger-pad a single drop of the solution is placed, and with a sharp needle, or pricker, the skin is pierced through the drop, so that the blood passes at once into the fluid, which is then received upon a slide and covered. The withdrawal of the corpuscles into the solution prevents the plaques from aggregating, and they remain as isolated and distinct elements. The amount of blood allowed to flow into the drop must not be large, and should be quickly mixed. In many respects the most suitable medium is osmic acid, ½–1 per cent., which has the advantage that by its use permanent preparations can be obtained. The various cells are at once fixed, and the plaques are, by this method, very well preserved. Good preparations may also be obtained by spreading rapidly a thin film of blood on a top cover, and then placing it at once in the osmic acid. Still another method is to dry the blood in the thinnest possible layer, and then fix with osmic acid or stain with methyl-violet, and mount in balsam. Kemp recommends placing the blood drop on a top cover, rapidly moving it about, and then washing off the superfluous blood with salt solution. The plaques adhere to the cover, while the red cells are swept away. The cover is then quickly put in osmic acid.

For the study of the plaques in the circulating blood, the mesentery or omentum plate must be employed, and a similar measure adopted to those used in the study of the circulation of the blood in mammals. The half-grown rabbit, white rat, or guinea-pig will be found best adapted for this purpose. The chief difficulties arise from the amount of fat which, in some instances, obscures the vessels, and the rapidity of the current may render it hard to see the plaque. But when, as in the omentum, a small transparent vessel is found, in which the current is slow, then with the red and colorless corpuscles the smaller plaques are also seen (Fig. 2). In Bizzozero's paper, and in the recent communication of

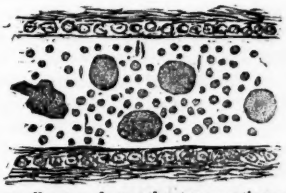
FIG. 2.



Plaques in circulating blood, omentum of guinea-pig. 18, 1, '83.

Eberth, full directions are given for the study of the plaques in the circulating blood. They are modifications of the original Sanderson-Stricker method (*vide* Sanderson's *Handbook*), which answers every purpose in the case of the guinea-pig, the omentum of which is a peculiarly suitable object. In the rapidly flowing current no plaques are distinguishable, but when the stream is slow they can be seen here and there in the still layer with the white corpuscles, while if the current becomes very feeble they tend to collect at the periphery with the leucocytes. In a small venule, where the stream is slow, and only a few corpuscles passing, the best opportunity is afforded of seeing the plaques. They may be well studied within the vessels in the recently killed animal, or in man, in portions of tumors, etc., recently removed. The subcutaneous tissues of the newborn rat afford perhaps the very best situation in which to study the plaques while within the vessels. The rat is killed with a snip of the scissors through the spine, and then portions of the mucoid connective tissue spread thin upon the slip, either with or without saline solution. In the thin transparent vessels, the plaques are very distinct, and they remain unchanged for hours. Perhaps there is no better mode of studying these forms, as the thin walls offer no impediment to the view, and the plaques are in their natural medium. In the subcutaneous tissue of man I have had several opportunities of examining the plaques in this way, and Fig. 3 represents

FIG. 3.

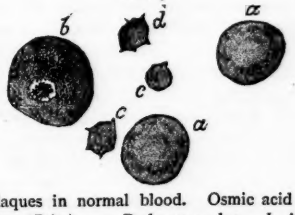


Plaques in small artery from subcutaneous tissue of scrotum of man, one hour after removal. Case of elephantiasis. 20, 11, '85. They had collected in numbers at this portion of the vessel.

them in a vessel of the tissue of the scrotum an hour after its removal. In the smaller vessels of the pia mater they may also be seen.

General Characters and Structure.—The plaques are minute elements circulating in the plasma with the other corpuscles, and possessing such specific and distinct

FIG. 4.



Isolated plaques in normal blood. Osmic acid 1 per cent.; one-twelfth im. (Zeiss). *a.* Red corpuscles. *b.* A white corpuscle. *c. c.* Plaques with slightly irregular margins. *d.* Plaque with faint granular appearance in centre as if nucleated.

characters that they must be reckoned among the normal histological constituents of the blood.

The plaque is colorless, with a uniform grayish-white appearance, homogeneous or very finely granular, and presents no differentiation in the delicate protoplasm of which it is composed. So far as my observation goes, it is always colorless.

The *size* is variable. In man they may be said to measure from 1.5 to 3.5 micromillimetres, or from about one-sixth to one-half the size of a red blood-corpuscle. The majority of them are from 1.5 to 2.5 μ. Oc-

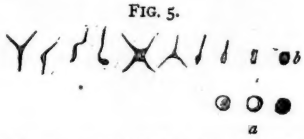
casionally a plaque may be seen measuring as much as 5 micromillimetres, but this is exceptional. When they are abundant, remarkable gradations in size may be measured between the smallest and largest forms. They have not the constancy in size of the red corpuscle. I think in man, when very abundant, the average size is slightly less than when they are not so numerous. They are stated to bear in size some relation to the size of the red corpuscle of the animal, but we need a more elaborate series of measurements to determine this. In the white rat they are slightly smaller than in man.

The shape of the normal plaque, as seen in the vessels, is a circular disk with smooth, well-defined margin. When slightly tilted it has naturally an ovoid appearance, and when seen in profile is as a narrow, straight rod or staff. Whether they are flat disks, or biconcave, as like red corpuscles, is really not easy to determine. I should say that the majority do not show a bilateral depression, but forms are sometimes seen which resemble in outline very closely a miniature biconcave disk. Alterations in form quickly occur when the blood is withdrawn; but the natural shape, as seen in the vessel, and also, as a rule, in Pacini's fluid, or osmic acid, is as here stated.

The plaque consists of a homogeneous, smooth, structureless protoplasm of a light gray color. In the unaltered condition no nucleus can be seen, but in the fluids used to conserve them the appearance is in the form of a collection of distinct granules, which may look like a nucleus. This will sometimes, in dried preparations, stain a deeper color in the hæmatoxylon than the remainder of the plaque, and it is regarded by Hayem as a nucleus.

Changes in the Plaques.—Outside the vessels the plaques are characterized by two peculiarities which have been a serious hindrance to their recognition as special elements of the blood, viz., the rapidity with which the protoplasm alters the tendency to adhere to one another and to any substance with which they may come in contact. Within the vessels, however, they do not seem to be more prone to rapid decay than the red or white corpuscles, and in the young rat, kept at ordinary

FIG. 5.



a

a. Changes in appearance of the plaque, due to separation of its protoplasm into a darker and clearer portion. *b*. Alterations in form of plaques examined in blood-serum and watched for three hours.

temperature, I have seen them in the vessels quite distinct and clear twenty-four hours after death. So also I have found them unaltered in the vessels of the pia mater in man, some hours after death; and, as I shall have occasion to show in the third lecture, they may in masses remain apparently unchanged for some time.

The substance composing the plaque appears homogeneous when first seen, but soon a change occurs, and the plaque presents a darker, more highly refractile portion and a clearer substance. Usually this darker portion is peripheral, but it may be central, and then is not unlike nucleus. It is as if a material had separated from the stroma or bases of the plaque, just as the hæmoglobin of the red corpuscle may do under the influence of reagents. The plaques undergo the most curious changes in shape, to the study of which I devoted much time in 1873. Within the vessels they are circular, but when at rest they not unfrequently become ovoid or prolonged, or slightly angular and crenated. These angular processes may increase greatly in length, and give a stellate appearance to the plaque. The changes in form are very fully described and figured in my original paper. These alterations are probably induced by changes in the external conditions, and are not amœboid or vital in character. The addition of serum to the blood drop, and the examination in a warm stage, afford the best means of studying the variations in form. Even within the vessels they may show these changes, and in the course of a few hours alter in a remarkable manner so as to be scarcely recognizable.

A very common change is the separation from the plaque of a mucin-like (?) material in the form of a pale sphere, which may remain attached to the cell or separate from it. When aggregated in masses, as in a slide of fresh blood, this process can be readily seen at the margin, and the field in the vicinity may be covered with these pale globular bodies. They result, doubtless, from the separation of some material from the substance of the plaque, and are identical with the spheres so often seen attached to spermatozoa in urine.

FIG. 6.

Alterations in the plaque while within the bloodvessels, sketched after three hours on the warm stage. 6, 4, '73.

In marked contrast to the stability of the plaques within the vessels is their rapid disintegration when withdrawn. At a low temperature this does not occur so quickly, and of this Hayem took advantage in his researches; but at the ordinary temperature, and in the examination of the blood without any reagent, the plaques unite with each other and undergo rapid change —a viscous metamorphosis, as Eberth[11] terms it. As I shall have occasion to point out, this is associated with the separation of fibrin which seems to arise first about the groups of plaques, as Ranvier noted in 1873, and he spoke of these little granulations—*grains sarcodique* of Vulpian—as centres of coagulation.

Action of Reagents.—This has already been referred to in the consideration of the best modes of examining and preserving the plaques. Water reacts upon them as upon the colorless elements, causing a swelling of the protoplasm and a rapid production of the pale spheres already described Dilute acid and saline solutions act in the same way. In three-fourths per cent. salt solution, or in the sodium sulphate solution for blood counting, they retain their outlines and do not so rapidly coalesce and disintegrate. Dilute potash solution causes speedy dissolution.

The aniline dyes stain the plaques as other protoplasmic bodies, and Bizzozero's fluid has the advantage of

tinting them and making them more distinct. In preparations by Ehrlich's method, the tint of the central portion of the plaques may be deeper than the periphery. Carmine appears to have no effect. For permanent preparations the dry method is the best, and they may be stained with hæmatoxylon, fuchsin, Bismarck-brown, or methyl-violet. The blood in osmic acid may be kept for some days if the cover-glass is carefully surrounded with paraffine. A solution of corrosive sublimate 1 : 1000 is also suitable for their preservation. The precise chemical composition of the plaques has not been determined, but from the similarity in most points of their reaction and behavior with dyes to the nuclei of cells, we may suppose their composition to be of a similar nature.

The Number.—The numeration of the plaques presents serious difficulties, on account of their extraordinary adhesiveness and the numbers now given, may be subject to revision when better methods are devised. In my own case the numbers range from 250,000 to 300,000 in the cubic millimetre, figures which correspond to those of Hayem. Full-blooded, plethoric individuals have rarely more than 250,000 per cubic millimetre. The variations in the same individual may be considerable during the day, and they seem increased after a full meal. Age has an important influence—in the infant and young child the number may be double that of the adult. In the newborn of all the mammals I have examined they were specially abundant. In advanced age they seem more numerous, particularly if the individual is weak and debilitated.

Until more extensive and more reliable counts are announced, we may say that the plaques in health number between 200,000 and 300,000, the ratio to the red being about 1 to 18 or 20, and to the white corpuscles 35 or 40 to 1. The numeration of the plaques is a much more tedious matter and requires far more patience than counting the red and white corpuscles. Rapidity is essential to success. I find the *compte globule* of Malassez rather more adapted than the Gower's apparatus, as the mixture can be more thoroughly and quickly made. The blood is got from a deep puncture and aspirated into the tube of the Potain mixer and then the Pacini's fluid or osmic acid is immediately drawn in. Frequently it will be found that, with the greatest care, the plaques have run together and the process must be repeated. It is essential, too, in the first aspiration of the blood, to reach the line at once; if the blood column goes beyond, it must be discarded and a fresh attempt made, as the time lost in accurately adjusting the column would be sufficient to allow the plaques to coalesce.

The Plaques in Disease.—In health the plaques are relatively scanty, and they aggregate into such small, scattered groups, that they do not necessarily excite the attention of the student, but every constant observer of the blood in states of disease must have marvelled again and again at the extraordinary number and size of the granule masses met with in certain cases. Led away by their constancy and peculiar character, writers have regarded them as specific and distinctive elements in certain affections (leukæmia, phthisis). From the able and comprehensive paper of Riess to the more recent one of Afanassiew, there have been very many observations on the frequency and significance of these bodies in disease, but we still lack careful and painstaking enumerations in the various acute and chronic diseases. A rough estimate of their increase or diminution may be made by any one well accustomed to their observation, but for scientific accuracy the hæmatocytometer must be used, and means must be devised to overcome the present serious source of error.

My own observations have been very numerous, and I have for years been in the habit of noting the paucity or abundance of these elements. In the absence, however, of systematic and reliable counts the notes are not worth much. The general results I may state as follows :

1. The plaques are increased in all chronic wasting maladies—cachexiæ—with or without fever.

This is very evident by examining in rotation the various patients in a hospital ward. The debilitated individuals, the subjects of phthisis, cancer, or other chronic wasting diseases, present a marked increase. In phthisis the number per cubic millimetre may reach 500,000 or more, and the ratio of the plaques to the red may rise as high as 1 to 5.

2. In acute sthenic fevers the plaques are not increased in the early stages, but as the disease advances, and the patient becomes weaker and more debilitated, the increase is usually marked. This is well seen in typhoid fever, in which the number of plaques during the first week may not rise above normal, while in the third and fourth week there is usually a notable increase.

3. In the so-called blood diseases the number of the plaques is variable. Many observers have remarked the great numbers in certain cases of leukæmia, but in others the increase is not apparent. So, also, in lymphatic anæmia. In some cases of Hodgkin's disease I have seen the plaques in extraordinary numbers. In profound anæmia the plaques may be very scanty. I have long noted, in cases of pernicious anæmia, that the clusters of plaques may be almost absent, or much more scanty than in health.

Distribution of the Plaques in Animals.—So far as our present knowledge goes, the plaques are constant constituents of the blood in mammals, and, with the exception of slight variations in size, the general features are the same in the various orders. My observations on this point have not been extensive, but I can speak of their presence in the blood of the dog, cat, mouse, guinea-pig, rabbit, sheep, ox, horse, pig.

They also occur in the ovipara, and here they are nucleated. Kemp states that in the blood of oviparous animals there is a nucleated corpuscle which is physiologically analogous with the plaque in the blood of mammals, and which behaves like it when the blood is drawn.

Origin.—Various explanations have been given to account for the origin of the plaques, and Kemp enumerates no less than seven different views. Perhaps the most prevalent idea, particularly among clinical physicians, is that they result from the disintegration and degeneration of the blood corpuscles, especially the leucocytes. This is really not unnatural, for the irregular clumps of plaques in blood examined in the ordinary way look very like—and, indeed, are—protoplasmic débris. But we know of no such process of rapid disintegration in the colorless corpuscles, which are remarkably stable elements, and even in their death and

decomposition never, so far as I can make out, produce structures similar to the groups of plaques. The fact that the formation of the *granular débris*, as the groups of plaques are called, can be prevented by drawing the blood directly into a drop of osmic acid (or Pacini's fluid), in which the elements are fixed instantly, should be sufficient to convince the most sceptical; but if it does not, the study of the plaques in the newborn rat will satisfy, I think, the most obdurate. The abundance and large size of the groups of plaques in a blood drop examined in the ordinary way, and the ready demonstration of the individual elements in the blood-vessels of the subcutaneous tissue, and the identity of these with the corpuscles at the edges of the groups, and with those in the osmic acid drop, render the conclusion irresistible that we are dealing with something quite independent of the colorless corpuscle.

I am unaware of a single observation corroborative of the view that the plaques result in any way from the degeneration of the red corpuscles. We need not consider the views that the plaques represent fibrin particles, or are depositions of globulin.

A majority of observers regard the plaques as independent elements in the blood, others agree with Hayem that they are young red corpuscles—hæmatoblasts—and a further discussion of this point will be best considered in the next lecture, when I speak of the regeneration of the corpuscles.

Historical.—I do not propose to enter into the literature of the blood plaque. This has already been done very fully by several German observers, and quite recently by Kemp, whose paper in the "Studies from the Biological Laboratory of Johns Hopkins University," will be readily accessible to all American and English students. In my original paper I have also given pretty fully the older references. We may conveniently divide the work which has been done in this department into three periods The first embrâces the time prior to the publication of Hayem's researches in 1877. The masses had been observed frequently, and the corpuscles had been studied, notably by Donné, Zimmerman, and Max Schultze. In 1874 I demonstrated the corpuscular nature of the granule masses, and showed that the bodies of which they were composed "were present as separate elements in the vessels, and showed no tendency to adhere together." In 1873 Ranvier[9] called attention to their possible association with fibrin formation. Riess and others had called attention to their increase in disease. The second period dates from the publication by Hayem, in 1877–78, of his researches, and to him really belongs the credit of establishing the histological position of these corpuscles as constant blood elements. It is curious that his careful observations met with very slight recognition among physiologists. The interest in the question had almost died out when, in 1882, Bizzozero, of Turin, published an exhaustive article in Virchow's *Archiv* upon the *Blutplattchen*, and their relation to fibrin formation. From this we date the third period, during which there have been already published eighteen or twenty essays, chiefly in Germany, and the most intense interest seems to have been aroused in the subject. The weight of histological evidence is strongly in favor of the views which I have here laid before you, but there still remains the greatest diversity of opinion as to the function of these bodies in blood development, and of their relation to the formation of fibrin, and upon these questions I shall have more to say in the second and third lectures.

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ORIGINAL ARTICLES.

ON THE EMPLOYMENT OF THALLIN IN FEBRILE AFFECTIONS.

BY J. P. CROZER GRIFFITH, M.D.,
ASSISTANT TO THE PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA.

TETRAHYDROPARACHINANISOL, or tetrahydroparamethyloxyquinolin, a hydrate of parachinanisol, was first synthetically prepared by Prof. Skraup, of Vienna, in 1884, and named by him "thallin," on account of the green color which its salts produce with the perchloride of iron (*θαλλος*, a green shoot).

It is a light powder of a pale yellow or almost white color, with a pleasant aromatic odor, resembling greatly that of the trailing arbutus. Its taste, however, is bitter, pungent, and disagreeable.

It is easily soluble in water, with difficulty in alcohol, and not at all in ether. The reaction of its solution is strongly acid. It is usually employed in the form of the sulphate or the tartrate of thallin, although other salts exist. Its chemical formula is $C_{10}H_{15}NO$. The reference to the paper containing a detailed description of the method of its manufacture will be cited below.

Von Jaksch was the first to experiment with it upon animals, and to appply it subsequently in medicine. Following him, various other clinicians made researches with the new drug, and reported their results, but up to the present time there has appeared, I believe, no published account of any clinical experiments with it, made either in this country or in Great Britain.

It was while watching its effect on fever, when given by v. Jaksch in the clinic of Nothnagel, before he had made his discovery public, that I first came to believe in the value of the drug as an antipyretic. And it is with the desire of bringing it more prominently and more favorably before the profession, that the investigations herein detailed have been made, and this communication written.

The first announcement from v. Jaksch was made to the *Wiener k. k. Gesellschaft für Aerzte*, in the fall of 1884, and published by him later. He followed this by several other papers on the same subject.

He shows that thallin is very similar in its effects to antipyrin, although in very much smaller doses; but claims that it is more rapid in its action, although the fall of temperature produced lasts for a shorter time. It is also less dangerous, inasmuch as it never causes collapse, as does the latter drug. Both agents may produce profuse sweating; and chilliness or rigors often occur with the subsequent rise of the temperature after the action of the medicines has ceased.

These conclusions he reached by giving thirty cases of various diseases, accompanied by fever, alternating doses of antipyrin and thallin. His investigations, throughout, were most careful and thorough. The usual dose of thallin as administered by him is four to fifteen grains, given at one time, and repeated in one or two hours if no effect is produced. The degree of reduction of temperature obtained varies somewhat, and the duration of the lowered temperature lasts usually but a few hours.

He states that it can be detected in the urine by the dark red color which is produced on testing with the perchloride of iron. Before testing, too, a peculiar greenish shimmer may be seen at the edge of the receptacle.

Alexander, after experimenting on fourteen cases, confirms the favorable report of v. Jaksch. He gives the medicine in the same doses whenever the fever exceeds 102° F. This usually reduces the temperature to 101° or 101.5°, where it remains for two or three hours. On its again reaching 102° the dose is repeated, the patient receiving the drug four or five times in the course of the day. Very profuse perspiration is often produced, especially in cases of phthisis.

Huchard finds the temperature always reduced by four to twelve grains of thallin, with but slight accompanying perspiration, although shivering occurs frequently. He believes that it probably lessens the fever by acting on the thermogenetic centre.

Dujardin-Beaumetz, while admitting that thallin is the most powerful of antipyretics, considers it a poor member of the materia medica. He adopts the opinion of Brouardel and P. Loye that it reduces the temperature by diminishing the respiratory power of the blood, and destroying the red blood corpuscles; and believes that antipyrin acts in an entirely different manner—*i. e.*, on the thermogenetic centre—and is much to be preferred.

This is the only really condemnatory criticism of the new antipyretic of which I am cognizant.

Guttmann's experience agrees with that of v. Jaksch, but he considers thallin to have many unpleasant secondary effects. Its action, too, he considers of too short duration, and he therefore gives the preference to antipyrin.

Ewald, on the other hand, says that the drug is safe, sure, and has no disagreeable secondary effects. He administers it in doses of four grains.

Landenberger reports seventy cases of various febrile affections to which he has administered the medicament. He gives it in from four to fifteen, usually eight grain doses, and in this way obtains a fall of temperature of even 5° or 7° F., accompanied by profuse sweating, but never by collapse or cyanosis. The effects continue five or six hours, before the mercury rises again. He usually administers it in wafers, to avoid the unpleasant taste, and has the temperature recorded hourly during the day, and every two hours at night.

He finds it much superior to antipyrin, kairin, and quinine, especially in reducing the temperature of erysipelas. It is also very efficacious in phthisis, but is apt to produce too profuse perspiration.

Stintzing, in employing thallin in Ziemssen's clinic, finds four grains sufficient to cause a fall of temperature of 1.5° to 3° F., lasting for three or four hours. The mercury then rises until it reaches the former or even a greater elevation. There is always more or less sweating after its use.

Mingazzini obtained better effects from a dose of eight grains than from smaller amounts. He never observed vomiting, collapse, or cyanosis, but sweating seldom fails to appear. He prescribes it either by the mouth, hypodermatically, or in clyster, and produces a fall of temperature equalling 1.5° to 4.5° F., and lasting four to eight hours.

Jaccoud has made a very careful series of investigations on seventeen cases. His average dose is six to eight grains, and his maximum fifteen grains, administered in wafers. The drug was always given at 11 A. M., and the temperature recorded hourly until 6 P. M. He believes that the initial dose should always be small, of three or four grains or less, since the effect appears to depend more upon the individuality of the patient, than upon the actual amount of the drug employed. The same observation is true of antipyrin. He finds that the temperature falls 3° to 9° F., and, having once reached its lowest point in one and a half to three hours, at once begins to rise again, there being no persistence of a minimum temperature. In two to four hours from the time the mercury begins its reascent, it attains its original elevation. Copious perspiration attends the reduction of the fever, and with the subsequent increase of the latter there is a sensation of chilliness and sometimes a rigor. His conclusions are that the salts of thallin are much to be preferred to antipyrin. With the latter drug the dose is much larger, the reduction of temperature not so great, and of no longer duration, the sweating more profuse, and chilliness and rigors more frequent. Then, too, there exists the disposition to the occurrence of the antipyrin exanthem. He considers that the liability to the development of collapse is equally great with both antipyrin and thallin. But the danger is much greater and more insidious from the former drug. Having once established the amount of thallin which can be given to a particular case, this dose can be employed without fear for as long a time as may be desired. But in the case of antipyrin the danger is renewed with every administration of the remedy. He has found by actual experience that a dose of antipyrin borne well on one day, may on another cause symptoms of collapse.

Pavay has employed thallin in seventeen cases and with a result almost diametrically opposed to that obtained by Jaccoud; much preferring antipyrin. Like v. Jaksch, he gave antipyrin and thallin alternately in a series of cases, and finds that of the two thallin produces much the greater sweating when eight grains of it are given. But it requires forty-five to sixty grains of antipyrin to lower the temperature to the same degree. The reduction of temperature after antipyrin lasts much longer, and rigors and collapse are not so likely to occur.

He disputes the statement of Dujardin-Beaumetz, and has repeatedly examined the blood without finding any alteration of the red blood-corpuscles after the use of thallin.

He gives four grains every quarter to half hour if the temperature exceeds 102° F. In one to two hours a fall of 3° to 5° F. is almost always obtained. He has endeavored in vain to check the profuse perspiration by administering one-sixty-fifth grain of atropia simultaneously with the antipyretic. After a dose of twelve grains of thallin he has observed collapse and more or less cyanosis. He agrees with Jaccoud that the drug is not to be invariably recognized in the urine by means of the perchloride of iron—a proof that it is largely consumed in the system.

Sara Welt, on the other hand, has never seen true collapse follow its use. The patient, although perhaps appearing somewhat cyanosed, feels well, and there is no diminution of strength. She has made in the medical clinic of Eichhorst, in Zurich, careful observations on the effects on the system of both thallin and antipyrin, administered to a large number of cases. Four grains of thallin are given hourly until apyrexia is produced. There is less profuse sweating and less frequent vomiting after the use of thallin than follow antipyrin, but chilliness or rigors occur more frequently.

Ehrlich and Laquer, in a recent paper on the employment of thallin in typhoid fever, advocate an entirely new method of administering it. They admit that thallin has two disadvantages: 1st. Its action, though rapid, is too transient. 2d. Hyperpyrexia with rigors is apt to follow the cessation of its effect on the system.

Antipyrin, on the other hand, has a more gradual fall of temperature, and a more lasting effect, with a slower reascension of the temperature curve. This is because thallin is absorbed with great rapidity, often affecting the system in ten or fifteen minutes, and its elimination begins in one-half to one hour. Antipyrin, on the contrary, is absorbed more gradually and does not appear in the urine until three hours after its administration (Maragliano).

Thus are explained the disadvantages of thallin, and also the *much greater danger* accompanying the exhibition of antipyrin claimed by Jaccoud, and fully agreed to by Ehrlich and Laquer.

They have limited their article to their experience with nineteen cases of typhoid fever, to which they gave thallin in small doses frequently and persistently repeated. Their method is as follows: Thallin tartrate is given in solution every hour during the day, and every two hours at night, and the temperature recorded every two hours. Six-tenths to one grain hourly is the initial dose, which, after two or three hours, is increased by one-tenth to one-eighth grain, and again by the same amount in two or three hours more.

In this manner the dose is gradually increased until a reduction of temperature of 1.5° to 2.5° F. is obtained, without, however, attempting to procure complete apyrexia, and carefully avoiding any unpleasant secondary symptoms. In this way they are enabled to escape entirely all rigors and excessive perspiration. They claim also that the subjective symptoms of the disease, especially those affecting the sensorium, are improved.

They have never observed collapse, and but rarely chilliness, which was caused by too large a dose. Vomiting occasionally occurs, due to the very unpleasant taste. As soon, therefore, as they have once determined the proper dose for a certain patient, they order the medicine in pill-form. The digestive organs and the kidneys were never affected, and the exanthem of antipyrin never observed. Occasionally slight sweating takes place, but without being annoying to the patient.

Though not prepared to make a positive claim to that effect, yet they are led to conclude from their observations that thallin probably has a specific action on typhoid fever, often ameliorating the symptoms and appearing to hasten recovery.

There are several other articles on the subject to which I could not obtain access.

There will be found below a list of references to the literature, which I have tried to make complete.

The abstracts of the views of the various investigators quoted above, exhibit a considerable difference of opinion. Dujardin-Beaumetz is the only one who really condemns the new antipyretic. Pavay thinks that it can never take a place equal to that of antipyrin; and Guttmann also prefers the latter drug. But, with these exceptions, the general verdict is that thallin is a most valuable, prompt, and safe antipyretic. The majority also claim that there is less profuse sweating following the use of thallin, and that the medicine is much safer and more rapid in its action than antipyrin. The weight of opinion, however, goes to prove its only disadvantage to be that the reduction of temperature after its employment does not last so long as that produced by antipyrin; but even this is contested by many of the writers mentioned.

I report below a series of cases illustrative of the value of thallin as an antipyretic. In most of these the drug was administered in a single dose, usually of four grains. The variety of diseases is unfortunately, but unavoidably, not so great as could be desired. The temperature was, when possible, recorded every hour; often this was not possible. It is not, as a rule, quoted here for those days upon which no antipyretic was given.

CASE I.—Phthisis with hectic and night sweats.

Nov. 19, 1885.—7 P. M., 103.4°; 8, 103.2 (4 grains of thallin sulph.); 9, 99.8; 10, 100.6; 11, 100.8; 12, 101; 1 A. M., Nov. 20th, 100.6.

27th.—8.30 P. M., 102° (4 grains of thallin sulph.); 9, 100.2; 10, 99.8; 11, 99.4; 12, 99.

28th.—1 A. M., 98.4°; 2, 98.2; 3, 98.6; 4, 99; 5, 99.2; 6, 99.

Dec. 9.—7 P. M., 102.4°; 9, 101 (4 grains of thallin sulph.); 11, 100.6.

10th.—1 A. M., 100°; 3, 99.4; 5, 99.8.

11th.—7 P. M., 102°; 9, 101.8 (4 grains of thallin sulph.); 11, 100.2.

12th.—1 A. M., 99.4°; 3, 99; 5, 98.8.

14th.—9 P. M., 101.4° (4 grains of thallin sulph.); 10, 100.8; 11, 100; 12, 99.

15th.—2 A. M., 99.4°; 3, 98.8; 5, 99.6; 6, 99.4.

27th.—2.30 P. M., 104.2° (4 grains of thallin sulph.); 3.30, 101.4; 4.30, 99.8; 5.30, 99; 6.30, 99.2; 7.30, 99.8; 8.30, 100.2; 10.30, 101.4.

Profuse sweating, usually followed the administration of thallin to this patient. For several days, however, she was very positive that she slept better and felt better after the use of the medicine. Later in the disease, the subjective symptoms were not so favorable.

CASE II.—Phthisis with hectic and profuse night sweats. Man, aged twenty.

Nov. 20, 1885.—8.30 P. M., 103° (4 grains of thallin sulph.: at 8.40, copious perspiration, but not so great as usual); 9, 102; 9.30, 100.6; 9.50, 100.

For three nights this patient took four grains of thallin with excellent results. Slept better, felt better, and perspired less than usual.

Subsequent trial of the medicine seemed to increase the sweating. A short time after taking the drug he was always conscious of a tingling, burning feeling throughout his whole body.

CASE III.—Phthisis with night sweats. Woman, aged twenty.

Nov 28, 1885.—8 P. M., 102° (4 grains of thallin sulph.); 10, 100.4; 11, 99.6; 12, 99.

29th.—1 A. M., 99°; 2, 98.4; 3, 98.2; 4, 98.4; 5, 98.4; 6, 100; 7, 100.

30th.—8 P. M., 102.4° (4 grains of thallin sulph.); 9, 101.2; 10, 101; 11, 99.6; 12, 98.2.

Dec. 1.—1 A. M., 98°; 2, 98; 3, 99.2; 4, 99.4; 5, 99.8; 6, 99.2.

2d.—7 P. M., 102° (4 grains of thallin sulph.); 9, 100.4; 10, 100.6; 11, 100; 12, 99.2.

3d.—1 A. M., 98.8°; 2, 98.4; 4, 99; 6, 99.2.

14th.—9 P. M., 102.6° (4 grains of thallin sulph.); 10, 101.4; 11, 100; 12, 99.8.

15th.—2 A. M., 99.2°; 3, 99.8; 4, 99.4; 5, 99; 6, 100; 7, 102.

26th.—9 P. M., 102 2° (4 grains of thallin sulph.); 10, 101.8; 11, 100; 12, 99.6.

27th.—1 A. M., 99.2°; 2, 98.8; 3, 100; 4, 100.4; 5, 100.3; 6, 100.8.

Jan. 2, 1886.—9 P. M., 102.6° (4 grains of thallin sulph.); 10, 100.4; 11, 99.4; 12, 99.

3d.—1 A. M., 99.2°; 2, 99.6; 3, 100.8; 4, 100.4; 6, 100.8.

CASE IV.—Pyopneumothorax; septic. Man, aged twenty-five.

Dec. 2, 1885.—9 P. M., 103.4° (4 grains of thallin sulph.); 11.30, 98.4 (profuse sweating and some chilliness and depression of strength).

3d.—3.30 A. M., 101°; 6, 101; 9, 103.6 (4 grains of thallin sulph.); 12.15 P. M., 100.2 (not much perspiration, but subjective symptoms not improved); 2.30, 101; 4.30, 101.8; 5.30, 102.

5th.—8 P. M., 104.6° (4 grains of thallin sulph.); 10, 100.8.

6th.—12.30 A.M., 100°; 2, 101.6; 6, 101.6; 7, 103.

23d.—9 P. M., 104.4° (4 grains of thallin sulph.); 10, 101.2 (free perspiration); 11, 100.4; 12, 100.

24th.—1 A. M., 100°; 2, 99.6; 5, 101.2; 6, 102.

Jan. 14, 1886.—9 P. M., 102.6° (4 grains of thallin sulph.); 12, 100.

15th.—2 A.M., 99.2°; 3, 99.2; 6, 101.6.

CASE V.—Typhoid fever in a girl aged fifteen; eighth day of the disease.

Dec. 4, 1885.—9.30 A. M., 105° (4 grains of thallin sulph.); 10 30, 102.4 (profuse sweat, pulse softer); 11.30, 102.6; 1.30 P. M., 105.6 (sponging with water and vinegar every hour); 6.30, 104.4.

5th.—9.50 A. M., 104.6° (4 grains of thallin sulph.); 10.30, 101 (perspiring; pulse soft); 11.30, 102; 1.30 P. M. 105 (2 grains of thallin sulph.: at 12.45 there was a slight chill, lasting half an hour, evidently ushering in the rise of temperature); 3, 102.6; 5, 105.7 (2 grains of thallin sulph.); 6.30, 103.8.

CASE VI.—Phthisis, advanced. Woman.

Dec. 5, 1885.—6 P. M., 101.5° (headache, gave 4 grains of thallin sulph.); 8, 97 (slight perspiration, feels better, and head aches less).

CASE VII.—Phthisis with nephritis and pyopneumothorax. Man, aged twenty-one.

Dec. 7, 1885.—5.15 P. M., 103.5° (4 grains of thallin sulph.); 5.45, 102.1 (at 5.40 a sensation of warmth over the whole body, and perspiration commencing; now profuse); 6.20, 100.4 (sweating entirely ceased); 7, 101.

CASE VIII.—Typhoid fever (seventh day) with pneumonia. Man, aged forty.

Dec. 8, 1885.—9.30 A. M., 103.4° (4 grains of thallin sulph.); 10.30, 100.8 (profuse perspiration); 11.30, 101; 1.30 P. M., 104.4; 2.30, 104.6 (4 grains of thallin sulph.); 3.30, 101.8 (profuse perspiration); 4.30, 102.1; 6.30, 104.4.

CASE IX.—Typhoid fever, second week. Man.

Dec. 18, 1885.—9.30 A. M., 102.4° (4 grains of thallin sulph.): 11, 98.4 (copious perspiration); 2 P. M., 102.5.

CASE X.—Phthisis. Woman, aged twenty-four.

Jan. 2, 1886.—9 P. M., 103.4° (4 grains of thallin sulph.); 10, 101.8; 11, 100.2; 12, 99.

3d.—1 A. M., 99.8°; 2, 99.6; 3, 101.8; 4, 101; 5, 101; 6, 103.2.

5th.—8 P. M, 103.4° (4 grains of thallin sulph.); 9, 101.8; 10, 99.4; 11, 98 4: 12, 100.

CASE XI.—Phthisis. Woman, aged twenty-eight.

Jan. 5, 1886.—1 P. M., 100°; 2, 100.8; 3, 100.6; 4, 101; 5, 101.4; 6, 102; 7, 102.4; 8, 103.2 (4

grains of thallin sulph.); 9, 101.2; 10, 99; 11, 98.2; 12, 99.2.

Feb. 1.—8 A. M., 100°; 8 P. M., 103.

2d.—8 A. M., 99.8°; 8 P. M., 102.6.

3d.—8 A. M., 99°; 8 P. M., 102.4 (administration of thallin tartrate, $\frac{6}{10}$ grain every two hours, commenced).

4th.—8 A. M., 98.4° ($\frac{1}{10}$ grain of thallin tartrate hourly); 8 P. M., 100.

5th.—8 A. M., 98°; 8 P. M., 103 (thallin stopped at 10 A. M., Feb. 5th, on account of vomiting).

The temperature during the administration of the drug was recorded hourly, and showed a very marked reduction of the febrile temperature. Through an oversight, these records were destroyed.

CASE XII.—Phthisis. Man, aged twenty-two.

Jan. 14, 1886.—7 P. M., 104.2°; 9, 104.8 (4 grains of thallin sulph.); 10, 102.2; 11, 101 (considerable sweating); 12, 100.2.

15th.—1 A. M., 99.2° (chilliness); 2, 99; 3, 98.8; 4, 99.8; 5, 101.8; 6, 99.8; 7, 104.

19th.—7 P. M., 104°; 9.30, 106.6 (4 grains of thallin sulph.); 11.30, 99.6.

20th.—12.30 A. M., 99°; 1.30, 99; 2.30, 99; 5.30, 100.2.

CASE XIII.—Typhoid fever, fifth day. Man, aged twenty-one.

Feb. 10, 1886.—8 A. M., 102.4° ($\frac{6}{10}$ grain of thallin tartrate every hour); 10, 102; 12, 103.6; 2 P. M., 104 (dose increased to $\frac{8}{10}$ grain hourly, and at night every two hours); 4, 104.4 (5 grains of thallin tartrate in one dose without effect); 6, 104.6 (the continuous use of $\frac{8}{10}$ grain continued); 8, 104.4; 10, 103.4; 12, 103.6.

11th.—2 A. M., 102.4°; 6, 103.2; 8, 102; 10, 101; 12, 102 (dose of 1 grain of thallin tartrate substituted for $\frac{8}{10}$ grain); 2 P. M., 103.8; 4, 103.2 (8 grains of thallin tart. in single dose, with but little sweating); 6, 102.2; 8, 101.4; 10, 102; 12, 102.2.

12th.—2 A. M., 102.6°; 4, 101.8; 6, 102; 8, 103; 10, 102 (dose increased to 1½ grains); 12, 103; 2 P. M., 103.4; 4, 102; 6, 103; 8, 103.4; 10, 103.2; 12, 103.2.

13th.—2 A. M., 103.2°; 4, 103.2, 6, 103.4; 8, 101.2; 10, 102; 12, 102.2; 2 P. M., 103; 4, 102; 8, 103; 10, 100.2; 12, 102.8.

14th.—2 A. M., 102.6°; 6, 103.4; 10, 101.4 (dose increased to 2 grains); 12, 103.2; 2 P. M., 102; 4, 102.6; 8, 103; 10, 103.4; 12, 102.

15th.—2 A. M., 104 6°; 4, 102.4; 6, 104.4; 10, 103.2 (thallin commenced 8 A. M., Feb. 10th, in continuous doses, now stopped); 12, 102.6; 2 P.M., 103 (20 grains of quinine); 3, 103; 3.30, 103.6; 4, 104; 4.30, 104; 5, 103.4; 5.30, 103; 6, 103; 6.30, 103; 7, 103; 7.30, 102.8; 8, 102; 8.30, 102.2; 9, 102,4; 9.30, 101.8; 10, 101.8; 12, 102.

16th.—2 A. M., 102°; 4, 102.2; 6, 102.2; 10, 101; 12, 103.4; 2 P. M., 103.4; 4, 104 (15 grains of antipyrin); 6, 101.2 (profuse sweat, more so than with thallin on Feb. 11th, *q. v.*); 8, 101.2; 9, 101.4; 11, 101.4.

17th.—10 A. M., 102°; 12, 103.2; 2 P. M., 103; 4, 103.4; 4.30, 104 (cold pack, with a slight temporary reduction of temperature); 8, 102. 4; 10, 103.4; 12, 102.

18th.—2 A. M., 104.6° (15 grains of antipyrin); 4, 102.4 (profuse sweating); 6, 104.4; 8, 102.6; 10.30, 103.4; 11.30, 103.4 (cold pack, lasting 25 minutes with a fall of temperature at 11.55 in axilla, but a rise in the rectum); 11.55, 102.6; 2 P. M., 103.4, 3.30, 104.4 (8 grains of thallin sulph.); 4.45, 100 (profuse sweating and considerable depression); 8, 103.3; 10, 103.6; 12, 102.6.

19th.—2 A. M., 103°; 4, 103.4; 6, 103.6; 7, 104.

This case is particularly interesting as being an example of the greater efficiency of both thallin and antipyrin, as compared with quinine and the cold pack.

CASE XIV.—Pneumonia. Boy, aged twenty-two months.

Feb. 13, 1886.—1 P. M., 102.1° (¾ grain of thallin tartrate); 2.15, 101.4; 4, 103.9.

14th.—12.30 P. M., 103.2° (¾ grain of thallin tartrate) 2, 102.5; 3.15, 103.9 (1 grain of thallin tartrate); 4, 100.8.

CASE XV.—Pneumonia. Boy, aged twelve.

March 12, 1886.—4 P.M., 104.4° (2 grains of thallin sulph.); 5, 103.4; 5.15, 103.8; 7, 105.2.

14th.—8 A.M., 104.4°; 4 P.M., 104.2 (1½ grains of thallin sulph.); 6, 100.6.

CASE XVI.—Pneumonia. Boy, aged nine.

March 21.—4.30 P.M., 106.5° (3 grains of thallin sulph.); 5.30, 104.2; 6.30, 101; 9, 105 (3 grains of thallin sulph.); 12, 100.

22d.—6.30 A.M., 105°; 12.30 P.M., 104.8 (2 grains of thallin sulph.); 2. 102; 4, 105 (2 grains of thallin sulph.); 5, 103 4; 8, 103.

Thallin in both Cases XV. and XVI. not only reduced the temperature greatly while producing only moderate perspiration, but diminished markedly the nervousness and restlessness and the rapid and violent heart's action. The condition of the sensorium was also decidedly improved, and the patients stated that they felt better. Sometimes natural sleep followed the use of the antipyretic. To both patients cold sponging was given hourly without any effect.

An inspection of the records given will show that thallin has been, without exception, efficacious in reducing temperature in the cases reported, and that this has usually occurred within one hour after its exhibition, although at times from two to three hours have been required before the full effect was obtained. Of course, no one claims that thallin or any other antipyretic is invariably successful.

The number of cases observed is sixteen, and the number of times the drug was administered, and the temperature recorded, exclusive of the continuous frequent exhibition of it in Cases XI. and XIII.; equals forty-four. The dose usually given was four grains, which I have generally found sufficient. The greatest reduction of temperature obtained equals 7° F., and the least, 0.4° F; the average being 2° to 4° F. The effect lasted a variable time, in the acute febrile affections not so long as in phthisis. In the latter

disease, a dose of thallin administered in the evening sometimes occasioned a lowered temperature throughout the night. As a rule, it required two to five hours before the mercury reached its former elevation, if, indeed, it did ascend so high. I cannot agree with Jaccoud that the persistence of the minimum temperature equals *nil.* Profuse sweating was frequent, chilliness occurred but seldom, and a slight rigor was seen once. I have never observed collapse, but have seen depression of strength occur in two instances; due, I think, to excessive perspiration. Vomiting was produced in but one case, caused probably by the unpleasant taste of the medicine.

As to the subjective symptoms, some of the phthisical patients especially complained greatly; principally on account of the copious sweating. Others, however, experienced no unpleasant effects, and some felt decidedly better, slept better, and had less profuse perspiration than usual. Two cases perceived a peculiar sensation of warmth throughout the whole body soon after the ingestion of the drug.

My experience with the continuous administration of small doses, is limited to Cases XI. and XIII. Although unsuccessful in the latter, I am inclined to believe that the remedy will often prove very efficacious when given in this manner.

Whether the simultaneous exhibition of atropia in sufficiently large doses will check the profuse perspiration forms not only an interesting clinical question, but bears upon the solution of the problem whether thallin simply causes a reduction of the surface temperature by evaporation, or acts upon the thermogenetic centre.

Thallin is undoubtedly a most powerful antipyretic, and the fact that decided depression of strength occurred twice in thirty-eight exhibitions of this remedy, indicated that it must be given with care to greatly debilitated subjects. It appears to have no particular action on the heart or on the respiration. As a rule, the rapidity of the respiratory movements and of the pulse is reduced at the same time with the degree of the fever, although not necessarily in proportion. With the question concerning the indications for the use of antipyretics in general, or the advisability of using them at all, these investigations have had nothing to do.

Thallin may be obtained wholesale from the Badische Anilin und Soda-Fabrik, Stuttgart, which manufacture it, or from their agents, Schott, Segner & Co., 28 Princess Street, Manchester, England, at a cost there of $2 per ounce. It can be obtained in this city, at the rate of $2.75 per ounce.

In conclusion, I wish to express my hearty thanks to Professor Wm. Osler for the material in his wards in the University Hospital, which he kindly placed at my disposal; also to Drs. F. A. Packard and G. M. Guitéras, for the great aid they have rendered me in preserving careful records of observations made there. Further to Dr. W. T. Learned, for the complete accounts of several cases in St. Mary's Hospital, to which he administered the drug; and to Dr. J. H. Fussell, for several valuable observations made in his private practice.

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123 SOUTH EIGHTEENTH ST., PHILADELPHIA.

RAPID DILATATION OF THE CERVIX UTERI FOR DYSMENORRHŒA AND STERILITY.[1]

BY A. H. GOELET, M.D.,
OF NEW YORK.

IN the first place, what class of cases demand this operation?

First, those in which the dysmenorrhœa is constant and severe, and in which stenosis or obstruction of the cervical canal is clearly defined. This includes acute flexion with obstruction. In this class of cases, the most intense pain is experienced before the flow makes its appearance, and gradually diminishes as the discharge is fully established. The explanation of this is, that the cavity of the uterus becomes filled with the menstrual fluid, and contraction occurs to expel its contents, producing the most excruciating agony. After the flow is established, some relaxation takes place at the point of obstruction, and it escapes more freely. When flexion exists, there is a partial straightening out of the canal. The congestion con-

[1] Read before the New York Academy of Medicine, Section on Obstetrics and Diseases of Women, March 25, 1886.

sequent upon this unnatural condition of the organ helps to intensify the suffering, and produces the severe backache and bearing down which precede and follow the flow.

These patients are, usually, extremely nervous and hysterical at all times, and more intensely so as the catamenial period approaches. Their digestion is impaired, and they suffer continually with backache, bearing down, and leucorrhœa. The symptoms, which may be slight before marriage, when the sexual organs are in a quiescent state, become more pronounced and agonizing after, when these organs are called upon to perform their natural functions. In some instances the pain is so unbearable that hypodermatics of morphia are resorted to, and, in time, these patients become habitual opium-takers.

The second class of cases demanding this operation, are those of acute flexion, where the probe can be easily passed after the proper direction of the canal has been ascertained, and no actual obstruction is apparent. The symptoms may not be so severe as in the first class, but the congestion of the uterus which precedes and accompanies the menstrual flow increases the flexion, and pain of the same character is the result. Here dilatation is done to overcome the flexion, and allow the introduction of the intrauterine stem, which serves to straighten the cervical canal, and hold it so, until nature can reëstablish the normal circulation and tone of the organ.

Third. Cases where little or no flexion exists, and there is only slight obstruction, but the passage of the sound through the internal os is attended with pain, and no other cause can be found for the existing dysmenorrhœa and sterility.

Fourth. A class of cases will present the following history, viz.: Previous to marriage the patient suffered little or no inconvenience. Sterility exists, and the dysmenorrhœa, which was at first only occasional and slight, has increased in severity. The sound enters freely without pain until it reaches the fundus, when severe pain is experienced by the patient; and there will be seen exuding from the os an albuminous fluid, in some instances so slight in amount as to be overlooked by a casual or inexperienced observer. This is a mild endometritis or uterine catarrh, which had no existence previous to marriage. But the congestion consequent upon the married state has lessened the calibre of the canal, which was barely large enough before, and has increased the normal secretions from the uterine cavity. As free escape is not afforded, they accumulate and are a source of irritation. Complete dilatation, if maintained, will alone cure some of these cases.

Unmarried women frequently suffer so acutely as to demand dilatation; and when the dysmenorrhœa is constant, persistent, and increases in severity, an examination should be made, and if stenosis or acute flexion exists, dilatation should be unhesitatingly done. I can see no reason why a young woman should be allowed to suffer because she is unmarried, when relief is assured by the operation, and delay may doom her to a life of misery from some incurable uterine disease.

The proper time for dilatation, is from one week to ten days after the cessation of the menstrual flow.

Much can be accomplished by preparatory treatment, in relieving the rigidity and congestion of the parts, by using every second day for a week previous to the operation, a tampon saturated with either glycerine or boroglyceride. A string being attached, it is removed by the patient in twenty-four hours, and the vagina thoroughly irrigated with hot water.

The instrument preferred is the Palmer dilator, modified in the following way, viz.: The blades are made thicker near the shoulder, and the outer surfaces flatter, to lessen the risk of injuring the cervical mucous membrane, and to prevent too much spring; and the shoulder is made more abrupt. The amount of separation of the blades is one inch, at a point corresponding with the internal os, when the instrument is in position. For greater convenience, the thumb screw attached to the handles has been transferred to the left side.

The operation is thus performed: The patient having been anæsthetized and placed on a table in a good light, with the second assistant, who may be a nurse, standing to the right of the patient (left of the operator), the speculum is introduced and the cervix exposed to view. Ordinarily the position on the back with a bivalve or trivalve speculum will answer every purpose; but for cases where much flexion exists the Sims's position and speculum are required. Unless it has been previously done, the sound is introduced first to ascertain the direction of the canal. Then, fixing the cervix, and drawing it down slightly with a tenaculum in the left hand, the dilator, held in the right, is introduced through the external os without much difficulty; but its progress is arrested at the internal os, where the obstruction generally exists. But steady, firm pressure exerted in the proper direction will usually overcome the obstruction, and the beak of the instrument jumps suddenly through the internal os. The shoulder on the blades limits the amount of penetration and prevents injury to the fundus. Where steady and firm, but gentle, pressure does not overcome the obstruction, I prefer to withdraw the instrument and pass successively applicators wrapped tightly with cotton, increasing the size until the dilator can be introduced without force. Harsh means cannot be too strongly condemned. I have never found it necessary to bore the external os with a pair of pointed scissors, and consider it a harsh and unnecessary procedure. Should an exceptional case present in which it was impossible to pass the probe, I should introduce a small laminaria tent and wait.

When the blades have been introduced as far as the shoulder, the handles are gradually brought together, the thumb screw being made to follow along and hold the advantage gained when the hand becomes tired, or the dilatation may be done with the screw alone. The amount of dilatation is usually the full extent of the instrument (one inch), but this depends upon the case. After a few moments the screw is loosened and the instrument is withdrawn. The canal is then cleansed of mucus by means of applicators wrapped with absorbent cotton, and a hard-rubber bougie (Hawk's), No. 13 American scale (20 French), is gently passed, followed by successive sizes up to 18 if the case require it. After this,

an applicator armed with cotton and dipped in liquid carbolic acid is passed through the cervical canal. A tampon of absorbent cotton saturated with the boroglyceride,[1] fifty per cent. with glycerine, is placed against the cervix and the patient is transferred to the bed to recover slowly from the anæsthetic. Besides possessing antiseptic properties, the boroglyceride depletes the tissues and relieves irritation.

The stem used in the after-treatment is of hard rubber two inches long and slightly curved, having a cup-shaped shoulder which hugs the cervix and remains in position better than the glass stem I formerly used.[2] It is tunnelled or perforated through the centre to allow drainage. There are three sizes, 10, 12, and 14 English, corresponding with sizes 13, 15, and 17 of the American scale. Its introduction is best accomplished by means of the sponge tent applicator, the end of which is made to fit in the perforation. By using this the stem can be introduced very nearly straight, even when there is considerable flexion. The curve in the instrument takes the place of the curve in the stem and allows the point of the stem to pass the angle in the canal with greater ease. By seizing the cervix on the side with a tenaculum, and pressing the stem firmly into the canal, carrying the handle of the instrument well back toward the perineum, its introduction is facilitated. In retroflexion the movement is reversed.

On the day following the operation the tampon is removed, the canal cleansed of mucus, and the hard-rubber dilators are again passed, after which the stem is introduced as described above and held in position by a similar tampon of cotton soaked with the boroglyceride. This is repeated every day, the stem being removed, cleansed, and replaced. After a week of this treatment, during which time the patient is confined to her bed, the stem is removed permanently and she is allowed to get up. In some instances the stem is introduced curved at first, and after the uterus has become accustomed to its presence it is straightened.

When compared with the more dangerous cutting operations for the same purpose, rapid dilatation has decided advantages and fewer objections. If done as described above, it is perfectly safe and effectual; and if the stem is used in the after-treatment to prevent recontraction, the results are both satisfactory and permanent.

Of eighty cases operated upon in this manner, it has not failed in a single instance to cure dysmenorrhœa. No unfavorable symptoms have followed any of the operations, if we except the feeling of uneasiness during the first few hours after, produced mainly by the efforts of the irritated uterus to expel the stem when this was used immediately after the operation. This discomfort is now avoided by delaying the introduction of the stem until the following day; and with this improvement the most sensitive patient may go through the whole treatment with little or no suffering. In addition to this advantage, which cannot be overestimated, the uterus is allowed to recover from the shock it has received and the danger (if there be any) is reduced to a minimum.

Of this number, twenty were unmarried, some of them pale, sickly girls who menstruated scantily. Some menstruated with great effort and the uterus was found to be undeveloped. Within a year these had developed into robust, healthy-looking women, and their menstruation had become normal.

Of the married who were capable of conception and whose histories were followed, one-third have conceived. I should add, however, that one-fourth of this number have been operated upon within the past six months.

The conclusions arrived at are:

First. That rapid dilatation is a perfectly safe, justifiable, and satisfactory procedure, free from the dangers which frequently follow the cutting operations, especially the occurrence of cicatricial contraction.

Second. If the stem be used in the after-treatment, recontraction does not occur, and the operation does not require repetition.

Third. The operation is demanded by the following conditions: viz., (1) Marked stenosis with or without flexion. (2) Acute flexion without actual stenosis, the obstruction existing only coincident with menstruation. (3) Slight stenosis as shown by the passage of the sound, dysmenorrhœa and sterility existing without other cause. (4) Mild endometritis from acquired narrowing of the cervical canal and lack of free drainage for the discharges.

243 West Fifty-fourth Street.

[1] See The Medical News, March 22, 1884, page 324.

[2] Ibid., April 18, 1885, page 431.

MEDICAL PROGRESS.

Specific Nature and Inoculability of Varicella.—D'Heilly and Thoriot have published in the *Revue des Maladies de l'Enfance* the results of an interesting investigation from which the following conclusions are drawn:

1. Varicella is inoculable, but the disease thus produced may appear suddenly and without prodromes.

2. Variola gives no immunity from varicella, nor does the converse of this obtain. One may succeed the other, even while the traces of the initial lesions are visible. It is certain that the two diseases may simultaneously exist in the stage of incubation in the same individual, and it is probable that they may be simultaneously inoculated.

3. Varicella offers no resistance to the "taking" of vaccine.—*Revue Médicale*, Jan. 16, 1886.

Effect of Transportation on Eggs.—Dr. D. F. Wright, in the *Bulletin of the Tennessee State Board of Health* for February 28, 1886, describes as follows a new "disease" of eggs.

There is a condition of the egg, very little known, which considerably impairs its sanitary value as an article of food. Soon after it became the practice to transport eggs in large quantities and to long distances by railway trains, it was found on their arrival that adhesion had taken place between the membranes of the yolk and those of the shell, so that the yolk could not be turned out of the shell unbroken. On examination by experienced pathologists this was found to be the result of true inflammation; the material of the adhe-

sion was found to be precisely the same as that of the plastic exudation in inflammation of the lungs or bowels. It will at first seem absurd to speak of inflammation in such an unformed mass as an egg; but this arises from our forgetting that, structureless and unorganized as it seems, the egg, even when fresh laid, is a living being, and capable of disease from external causes. The cause of this inflammation is undoubtedly the shaking and friction from the motion of the cars, and it cannot but render the egg more or less unhealthy, as the products of inflammation can never be as salutary in food as those of healthy growth.

THE MEDICO-LEGAL SIGNIFICANCE OF HÆMATOMA OF THE STERNO-CLEIDO-MASTOID IN THE NEWBORN.—In an elaborate original article in the *Centralblatt f. Gynäkologie* of February 27, 1886, KÜSTNER presents the following conclusions:

1. Hæmatoma of the sterno-cleido-mastoid is not a result of extension or stretching, but of torsion of the neck.

2. Inasmuch as severe torsion of the neck may occur in spontaneous delivery, and in foot or breech as well as in head presentations, hæmatoma also may occur under these conditions.

3. Hence it is not permissible to conclude from the existence of a sterno-cleido-mastoid hæmatoma that manual or instrumental aid has been applied in the delivery.

SCOPOLEINE AS A MYDRIATIC.—PIERD'HOUY describes the alkaloid of *scopolia japonica*, and claims for it a stronger mydriatic action than is obtainable from atropine. Clinically the use of the drug was found to be exempt from the discomforts observed in the exhibition of atropine. Its action is described as being very rapid, and, therefore, adapted to cases in which an immediate ophthalmoscopic examination is desirable.—*Les Nouveaux Remèdes*, Feb. 1, 1886.

RULES FOR PREVENTING THE PROPAGATION OF TUBERCULOSIS.—The Council of Hygiene of the Department of the Seine has just adopted and published the following series of instructions:

"The most active agent in the transmission of tuberculosis exists in the sputa, which should, therefore, never be deposited on the floor or on the linen, where it may be converted into a dangerous power.

"The patients in question must be instructed to expectorate in vessels containing sawdust; the contents of these vessels must be daily thrown into the fire, and the vessels themselves washed in boiling water at least once daily.

"The furnished apartment of a phthisical patient, especially in case of his decease, must be completely disinfected, together with all bedding, and the clothing of such a patient must not be used until it has been subjected to the action of steam."—*Gaz. Méd. de Paris*, Feb. 27, 1886.

HEPATIC ORIGIN OF UREA.—DR. D. W. AITKEN describes, in the *British Medical Journal* of February 6, 1886, the following interesting case, the direct bearing of which upon the question of the source of urea is evident:

Early this month (January) I was called to see a boy who had, the day previous, received a rather severe blow upon the right lobe of the liver. When seen, he was complaining of much pain in the right hypochondrium. The skin was slightly, and the conjunctiva distinctly, jaundiced. The stools were pale, while the urine was bile-colored, and gave the bile reaction with nitric acid; there was no fever. But herein lies the important matter. The urine was highly alkaline. On the addition of nitric acid, there was such violent effervescence, that the froth was forced out of the test-tube, although the urine was not much more than one inch deep. I got my friend, Dr. Drinkwater, to examine the urine carefully. He reports that the alkalinity was due to ammonium carbonate, and, on estimating the urea, he found only three per cent.

This evidence seems to point strongly to the liver as the seat of production of urea. Dr. Graves has already reported several cases of absence of urea which he believed to be represented in the urine by the ammonium carbonate, but here we have a history of the organ involved.

TUBERCULAR CONTAGION.—At a recent meeting of the Société Médicale des Hôpitaux, M. VALLIN, in the name of the Committee on Phthisiology, reported as follows: The Committee had last year addressed a series of questions relative to the contagious nature of tuberculosis to 10,000 physicians, and answers had been received from only 83.

Of the 83 responses, 37 favored and 37 contested the existence of the contagium; 7 were unable to form an opinion, and 2 gave uncomprehensible responses.

The number of actual observations presented was 439. Of these, 213 were favorable to the contagion, and 226 hostile. On the first series of the 213 cases the following conditions of transmission were operative:

107 between married couples; 71 between near relations; 18 from child to parent; 16 between distant relations; 1 from man to dog.—*L'Union Médicale*, March 6, 1886.

INTRAVENOUS INJECTIONS OF IODINE.—VAN DER HEYDEN has shown that large quantities of iodine may be injected into the veins without injury. The solution used is of the following composition:

Iodine	1 part.
Sodium iodide	2 parts.
Distilled water	7 "

The dose is two fluid-drachms. The treatment was first applied in a case of gastric fever of typhoid type, in which the temperature was 104° F., with a lasting fall of temperature. In two cases of incipient cholera good results were also obtained; in another, in which the algid state was pronounced, the injection was inefficacious.—*Les Nouveaux Remèdes*, March 1, 1886.

INDUBITABLE CONGENITAL TUBERCULOSIS.—An eight months' fœtus was taken from a cow, the subject of advanced tuberculosis, by DR. JOHNE. The placenta and uterus were free from tuberculous lesions, but in the lower lobe of the right lung a nodule the size of a pea was detected containing four caseous centres. The bronchial glands were congested and also tuberculous. The liver contained numerous gray granulations. Microscopically the tubercular structure was confirmed; masses of epithelioid cells with giant corpuscles containing tubercular bacilli were discovered.—*Lancet*, March 6, 1886.

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SATURDAY, APRIL 3, 1886.

THE PROPOSED BUREAU OF PUBLIC HEALTH.

IN THE MEDICAL NEWS of February 6, 1886, p. 148, attention was called to the prospects of National Public Health Legislation in the present Congress, and to the provisions of a bill prepared by the representatives of the American Public Health Association and of the Association of State Boards of Health to create a Bureau of Public Health in the Department of the Interior. As the Committee on Public Health had been abolished by the New Rules of the House of Representatives, this bill was referred to the Committee on Commerce, and, on March 23d, this Committee reported the bill with a few unimportant amendments, so that it is now on the calendar of the Committee of the Whole.

The bill, as reported, provides that a Commissioner of Health is to be appointed from civil life by the President, by and with the advice and consent of the Senate. The annual salary of this Commissioner is to be four thousand five hundred dollars. He is to collect and publish information relating to the public health, and as to the sanitary condition of ports and places at home and abroad, and, with the approval of the Secretary of the Interior, he is to make investigations both in the United States and, if necessary, in foreign countries, into the nature, origin, and prevention of contagious and epidemic diseases. The bill appropriates seventy-five thousand dollars to carry out its provisions, and repeals the act creating the National Board of Health.

There seems to be a fair probability that this bill may become a law, the chief danger of its failure is that of being crowded out in the press of business. That the country needs some such department of Government is very certain, and, although some opposition to this particular plan may be developed, it does not seem probable that anything can be proposed which will be more likely to secure unanimous approval.

As we have previously explained, there is not the least probability that Congress will grant any funds to the National Board of Health, and, that being the case, its friends admit that the sooner it ceases to exist the better, in order to make it possible to try some other method of obtaining the desired end. We can see no ground for objection to the proposed law, except possibly on the part of some enthusiastic sanitarians, who may think that it does not give the Commissioner any power, but, if this be a fault, which we do not believe, it is at all events a fault on the right side.

TUBERCULOUS INFECTION OF WOUNDS.

SINCE Volkmann called attention to the importance of studying the relation of tuberculosis to a variety of surgical affections, a large number of disorders which had previously been classed under other names, and generally and vaguely regarded as scrofulous, have come to be looked upon as essentially tuberculous. This is especially true in regard to many chronic inflammatory diseases of the bones and joints; so that it is now well recognized that the tuberculous process attacks the hard parts as well as the soft parts of the body. As a consequence, the presence of tubercles is suspected, and the detection of the bacillus tuberculosis is sought for in many cases with the result of confirming the analogy between tuberculosis of these tissues with that of the soft tissues, which has become so prominent a feature of the study of diseases of the bones and joints.

A very serious subsidiary question to the whole study of tuberculosis is that of accidental infection. In regard to the lungs and intestinal canal, this question is considered settled by many students of the subject. They have no doubt of the reality of infection by inoculation. This conclusion is not so evident to all, but it must be admitted that it has a very high degree of probability, and may be recognized without laying one open to the charge of hasty generalizing. In regard to the bones and joints, the matter is not yet so clear. The evidence in favor of the assumption that these tissues are sometimes infected by inoculation, is not yet strong enough to warrant very positive conclusions.

In 1882, KÖNIG reported a case in *Die chirurgische Klinik zu Göttingen*, Leipzig, 1882, p. 180, in which, after osteotomy for rachitic curvature of the bones of the leg, done with aseptic precautions, local tuberculosis followed, and the patient died in two months, the autopsy revealing tubercles in the ulcer at the seat of the wound, in the bone, in the

lymphatic glands of the thigh and iliac fossa, as well as in the liver, omentum, intestines, and lungs.

TSCHERNING has also recorded a case of accidental inoculation following a traumatism (*Centralblatt für Chirurgie*, June 20, 1885). Both of these cases are open to doubt as to their real nature, although they deserve consideration as evidence in this matter. Most recently KRASKE has recorded two cases in which he believes that tuberculosis was due to inoculation in a surgical wound (Ueber tuberkulöse Erkrankung von Wunden, *Centralblatt für Chirurgie*, Nov. 21, 1885). In this paper the author refers to the comparative frequency of the reappearance of tuberculous disease after incomplete removal of an affected part, and to the fact that such a recurrence has never been observed after unquestionably complete removal—as by amputation through healthy tissue—and to the other fact that there is no reliable record of the occurrence of tuberculosis after an operation in an individual not affected with, or predisposed to, tuberculosis.

His first patient was a boy, eleven years old, with an excellent family history, except that a sister was consumptive. The boy suddenly fell ill with fever of a high grade, which was diagnosticated to be typhoid (typhus). Symptoms of osteomyelitis soon appeared, and an abscess formed over the right thigh, which was opened, and from which a sequestrum was removed. Two years afterward Kraske found him with two fistulæ communicating with diseased bone, but without any sequestrum. He cleared out the fistulæ and the cavity in the bone, and dismissed his patient from the hospital at the end of two weeks, with one fistula healed, and the other closed, except the opening, which had been occupied by the short drainage tube, and which was granulating well. Seven months afterward the boy was brought back, with the second fistula still unhealed, and with pronounced tuberculosis of the bone and of the surrounding parts. In the tissues now removed miliary tubercles and giant cells, as well as a few bacilli, were found.

His second case was that of a boy, ten years old, with clearly tuberculous antecedents. His illness began with high fever and delirium in November, 1884, after a fall upon the left knee. Two abscesses formed above the knee in three weeks. In June, 1885, the boy came under Kraske's care. At this time he presented a badly united fracture of the lower part of the left femur, in regard to which no history could be obtained. He had also a fistula on the outer side of the thigh, communicating with a movable sequestrum. A second fistula on the inner side of the thigh led down to bare bone. This fistula, in contrast to the other, which was granulating, was surrounded by thin, undermined skin, and was not granulating. When operated upon, this fistula was found to be tuberculous. The other one was not, but led down to bone showing unmistakable evidence of osteomyelitis. About six weeks after the operation on both fistulæ the patient was dismissed, with the injunction to return. Kraske says the wounds granulated well, but does not state that they were entirely healed when he sent the boy away. The subsequent course of the case may be looked for with some interest, and it is to be hoped that the same surgeon may have another opportunity to observe and report upon it.

In commenting upon these two cases, Kraske asserts positively that the previous history and the appearance of the diseased parts leave no doubt that both were originally cases of acute osteomyelitis, and he believes that the development of tuberculosis was due to infection by inoculation. He attributes the tuberculous infection in the first case to inoculation of the wound, on account of the appearance of greater intensity near the surface, and the diminution in intensity in the deeper part, which is analogous to the appearance presented in secondary cheesy infiltration of the ends of bones when their cartilage has been destroyed, and which was so markedly the case in his second patient. In the second case, tubercle bacilli were found in the scrapings of the *outer* part of the fistula which presented the appearance of tuberculosis, but not in any of the *débris* of its deeper part, nor of that from the other fistula which communicated with the sequestrum cavity. Kraske argues that the inoculation of wounds with the virus of tuberculosis is not so uncommon as it is generally supposed to be, citing cases recorded by Karg and by Riehl, as well as that of Tscherning, which we have already mentioned. In the first of his own cases the patient was nursed and the wound dressed daily in the same room with his consumptive sister, and in this room the dressings for his wounds were kept. This, Kraske not unreasonably supposes, would furnish an easy way of explaining the manner in which inoculation took place. In conclusion, he suggests the question, whether or not an acute osteomyelitis may strongly predispose an individual to infection, who would not otherwise be liable to it?

From this epitome of the paper of Kraske, it will be seen that he makes out a good *prima facie* case for his opinion; but it is not conclusively proved. Although there is abundant evidence of the possibility of experimental inoculation of tuberculosis, there is, in our opinion, room for great doubt as to the occurrence of accidental inoculation. A comparatively small number of reported cases in which the assumption that infection has taken place in this way seem plausible, but they cannot overturn the apparently strong argument against it, which is furnished by the general experience, medical and surgical, in regard to

the occurrence of tuberculosis, and the special experience in hospitals for consumptives, such as is furnished by the reports, often cited, of the Brompton Hospital. And even in these interesting cases reported by Kraske, we cannot see why he should assume that the first occurrence of the deposit of tubercles in the outer parts of certain fistulæ points so surely to the entrance of the *materies morbi* from the outside. It cannot be doubted, from the enormous number of cases of tuberculosis occurring in closed cavities, that something in the individual leads to their development. It seems equally certain that tuberculosis develops in the first place at a *locus minoris resistentiæ*. Now in such cases as are cited by Kraske, is it unreasonable to assert that the parts near the surface may have been, and probably were, the points of least resistance? If they were, then what he considers a cause was an effect. The introduction of tubercle in the outer parts of the fistulous tracks was not the cause of their diseased state, but their weakened and diseased condition was the determining cause of the formation of tubercles first at that particular spot.

We say this, not with the design of denying the correctness of Kraske's opinion, or of impugning his candor, or of depreciating his ingenious argument, but in order to invite a further critical study of the question of the inoculation of wounds with tubercle —a question than which there are few more interesting in medicine and surgery, and one which is of the utmost importance for mankind. There are abundant opportunities in general and in hospital practice to follow up the study of this question, and if we succeed in prompting some of our readers to use these opportunities we may hope, before long, to have contributed something more positive to its solution.

FAULTS OF HOUSE DRAINAGE.

THE illustrations in *The Sanitary Engineer* of March 18, of specimens of defective and dangerous plumbing-work removed from dwelling houses, some of them costly edifices, which have been preserved by the Master Plumbers' Association of Philadelphia for purposes of instruction, point forcibly to the necessity of efficient sanitary regulation and supervision of house drainage and plumbing in all their details. These examples represent only a few of the defects which are constantly encountered in overhauling old plumbing-work, and their publication will confer a benefit upon the public by drawing attention to this important subject.

Nuisances caused by faults of house drainage are of a serious character, because the effects are exerted directly within the house. The modern plan of disposing of solid and liquid excreta and the bath and kitchen waters by means of a system of pipes connected with a common drain leading into the public sewer or a cesspool, exposes the inmates of the house to dangers to health incident to faults in the drainage arrangements themselves, and to a close connection with the sewer or depository of sewage. Bad materials, inferior apparatus, and unskilful construction may defeat the object for which the system of drainage is intended, so that the air of the house and the soil upon which it stands become contaminated by the escape of gases from foul waste- and soil-pipes or offensive sewers, and by leakage of liquid filth through disjointed pipes. Water-closets, baths, sinks, and washstands in the interior of the house, the latter often within the bedrooms or in their close neighborhood, are brought in more or less direct communication with sewers, and are often so many outlets for foul and even poisonous vapors that collect within them. The ignorant or negligent arrangement of overflow-pipes, the want of proper traps, traps allowed to become dry by disuse or leakage, the careless misplacement of traps of the movable kind, afford so many ways for the entrance of sewer air, an accident which is all the more certain to occur when there has been neglect to provide ample soil-pipe ventilation. Water-closets of bad design and construction, which retain the filth and become obstructed from this cause, as well as from insufficient flushing, are a constant source of offensive odors.

Another danger arises from injudicious connection of the service-pipe with the water-closet for flushing purposes. It is a very common occurrence, even with the constant system of water-supply, for the flow of water on the upper floors to be cut off by loss of pressure caused by turning on a cock in the basement or on the lower floor. Should the closet-pan be full and the valve open when the flow is stopped, it is possible, and highly probable, that foul air and even fluid filth will be drawn into the service-pipe and defile the water that may be immediately afterward used for drinking purposes.

House drains, which are very frequently located immediately under the house, may be the means of polluting the soil and foundations, should any defects exist in their construction. By unskilful construction, or by subsequent careless use, or want of repair, the sewage of the house, instead of passing freely and continuously into the sewer, becomes effused into the basement through broken or disjointed pipes. In consequence of the escape of the liquid parts of the sewage, obstructions form, which, in time, block up the pipes. This occurrence is frequently not detected until, after an unusual discharge of liquid matter which the saturated soil is not able to absorb quickly, the sewage makes its appearance at the lowest fixture in the house by an overflow. Where water escapes, gases will also escape, and through the same breaks and misplaced joints sewer-air will pass into the soil, adding to its impurities, which, in the form of foul air, are drawn directly

into the basement, and thence distributed all over the house by the ascensional force of heated air.

Neglect to make use of an intercepting trap on the main drain between the house and the sewer and to provide for the free circulation of fresh air throughout the drain and soil-pipe are faults which cannot be too severely condemned. Concealment of the pipes within partition walls or beneath basement floors gives finish to the work, but it prevents prompt detection of defects and makes repairs difficult and expensive. Other faults might be enumerated, but the selection made should be sufficient to indicate the importance of municipal regulation of house drainage and plumbing-work according to established rules and the principles of sanitary science.

EXPERIMENTAL TRANSFUSION.

IT is now generally recognized that many of the conditions in which the operation of transfusion of blood has been regarded as essential, may be successfully treated in other ways. Thus it is admitted that the collapse following severe hemorrhage is due not to a loss of blood *per se*, but to a purely quantitative loss of fluid vascular contents—a loss which may be supplied by the intravenous injection of salt solution. Nevertheless, in spite of its dangers, occasions arise in which transfusion is indicated, and in view of the growing disfavor with which the operation is now regarded, much interest attaches to some recent experiments of BIZZOZERO and SANQUIRICO, recorded in the ninth volume of the *Arch. per le Scienza Med.*

In the dogs which were the subjects of these experiments, both the numerical proportion of the red corpuscles and the percentage of hæmoglobin were first ascertained. Blood in varying amounts was then withdrawn, and an equal quantity of defibrinated dog's blood transfused by the jugular vein. In periods of from fifteen minutes to eighteen days the blood of animals thus operated upon was investigated, and the results compared with those of the preliminary examination. In a second series of experiments, one-half of the total blood of the animals was withdrawn, defibrinated, filtered through linen and returned to the veins of the animals from which it was taken. This procedure was ten times repeated, so that each corpuscle of the animal was subjected approximately five times to this rough handling. Before and after this series of experiments the same close examination of the quantitative relations of corpuscles and hæmoglobin was instituted, with the result of showing that in no case, in either series, was a noteworthy effect produced.

These observations lead to the conclusion that not only is the red corpuscle remarkably resistant to rough treatment, but that the transfusion of the defibrinated blood of animals of the same species is not injurious.

SOCIETY PROCEEDINGS.

COLLEGE OF PHYSICIANS OF PHILADELPHIA.

Stated Meeting, March 3, 1886.

THE PRESIDENT, S. WEIR MITCHELL, M.D., IN THE CHAIR.

DR. THOMAS G. MORTON reported

A CASE OF SPINAL CURVATURE THE RESULT OF UNRECOGNIZED ASYMMETRY IN THE LOWER LIMBS.

The patient, aged twenty-four, was a puny boy until about the age of fifteen. He then grew rapidly and gained his height, which is now five feet eleven inches, in the course of fifteen months. He has never been sick in his life, with the exception of the ordinary ailments of childhood. While growing rapidly, he noticed when lifting a stone some pain upon the right side. He has never experienced pain, except when lifting weights, never while lying down. He has been a student of medicine for two and a half years. Sitting on hard benches has caused considerable spinal ache. A year ago the diagnosis was made of serious necrosis of the lower dorsal and lumbar vertebræ. For this a plaster jacket was applied. During the past four or five years, there has been a constantly increasing lateral curvature. On examination Dr. Morton found a marked spinal curvature with lameness, and great asymmetry in the length of the lower limbs. He found it necessary to use a block an inch and seven-eighths in thickness, to bring the right limb to its proper length as compared with the left. With this elevation, the spinal curvature almost entirely disappeared. It has been a little difficult to determine whether, at the time he commenced to grow more rapidly, there was any involvement of the spinal nerves which impaired nutrition of the affected side, which involved not only the upper part of the body, but the lower part as well. Dr. Morton's experience in lateral curvature is, that in the absence of asymmetry of the lower limbs almost all curvatures arise from some morbid condition of the spine, as seen in infantile paralysis. There is generally more or less muscular atrophy and permanent deformity in cases of marked lateral curvature. This is seen in the diminished size of the upper and lower extremities of the affected side in most of these cases. It is barely possible that when this patient commenced to grow, at the age of fifteen, development did not take place in the right side and lower extremity, but against that theory examination shows that the thigh and calf muscles are equally developed, the only variation is the unequal lengths of the limbs. He, therefore, believes that this want of development is congenital. The patient has always had difficulty with the heel of the shoe upon the right side, which would wear out differently from that of the other.

The patient now has no spinal tenderness, except when in the deformed position. He is now unable to stoop very well, but before the application of the plaster jacket, less than a year ago, all of the spinal movements were normal, and he was quite a gymnast. He ascribes the present condition to the use of the jacket. The unnatural pressure, perhaps, led to a partial absorption of the intervertebral cartilages upon the right side, and

this may have caused more or less fixation of the vertebræ.

In many cases asymmetry in the lower limbs produces a slight amount of lateral curvature with pain. A careful measurement of the limbs will detect this at once.

DR. W. W. KEEN said: In standing with his foot on the block, the patient's right buttock seems higher than the left. This appears to be confirmed by examining the line of the anterior superior process of the ileum. The deformity appears to be overcorrected by the block one and seven-eighths inches high, and the shortening less, therefore, than was stated. He should like to ask Dr. Morton whether there is any explanation with reference to the causation of the trouble.

DR. DE FOREST WILLARD said: If this be simply a case of lateral curvature, how does Dr. Morton account for the marked rigidity? Rigidity is rare in lateral curvature except in the late stages. It is difficult to determine in this case whether rotation has occurred, on account of the inability of the man to stoop. The pressure of a gypsum jacket for so short a time should have produced relaxation and atrophy rather than stiffness.

DR. THOMAS G. MORTON thought that the want of symmetry in this case is congenital. With reference to the slight overcorrection of the deformity, it may be that this block is a little high, but the only way we have of noting when the asymmetry is overcome is by the eye, and the absence of lameness in walking.

Lateral curvature of the spine frequently occurs in hip-joint disease. One reason that it does not occur in many cases is that the shortened limb is provided with a proper shoe apparatus. He did not say that absorption of the intervertebral substance had occurred, but he thought it possible. It is probable that in the course of six months or a year the now slight unrectified curvature may disappear. In order to support the spine in every direction, the patient wears an ordinary spinal brace. The spine was perfectly pliable until the plaster jacket was applied and worn a number of months. This may have had some influence in stiffening the spinal column. The patient has never had any symptoms indicative of Pott's disease.

NEW YORK COUNTY MEDICAL ASSOCIATION.

Stated Meeting, March 15, 1886.

THE PRESIDENT, C. A. LEALE, M.D., IN THE CHAIR.

DR. HERMAN M. BIGGS read a paper on

THE ETIOLOGY OF RABIES, AND THE METHOD OF M. PASTEUR FOR ITS PREVENTION.

Much study, he said, has been given to this disease, perhaps the most terrible one to which the human or animal organism is subject, as has been the case with most affections when the causation was involved in obscurity. These investigations, however, have resulted only in the presentation of many hypotheses, without establishing a single condition or circumstance which can bring about or predispose to the development of the disease, excepting only the contagious principle as transmitted from rabid animals. Many observers have, therefore, expressed their belief in the occasional spontaneous origin of rabies, among whom is Fleming, the most able of the recent English writers on the subject, who says that there are few nowadays who are not convinced that it will occasionally appear in a spontaneous manner and without any exciting cause.

In support of this view he referred to the appearance of the disease in an epizootic form in countries where it has been previously unknown, and when its appearance could not be traced back to any foreign source, as was the case in Peru, in 1803. Again, it has been observed not infrequently that in certain countries which have been free from the disease for long periods of time, it suddenly appears in almost an epidemic form, and after a short time becomes again apparently extinct.

But whatever disagreement there may have been among writers as to the spontaneous origin of rabies, there has always been the greatest unanimity as to its contagious nature. More recently it has been almost fully established that this contagious principle, whatever may be its nature, is the only "evident, efficient, and incontestable cause." The occasional spontaneous development of the disease in certain of the carnivora, as advocated by many distinguished veterinarians, must, he believed, be entirely rejected in view of the facts recently demonstrated with relation to the germ diseases, and he accepted absolutely the conclusion that "this disease is maintained and spread solely by its contagious principle, and that there are no other causes in operation."

It is a matter of the greatest importance that the fallacious ideas so prevalent among the laity, and to no small extent among the profession also, in regard to the influence of climate, season, hunger, thirst, food, pain, anger, ungratified sexual desire, etc., as predisposing or exciting causes, should be corrected. There are no better or more reasonable grounds for believing that any one or all of these influences combined can bring about the development of a single case of rabies, than that unfavorable sanitary conditions can produce smallpox when the specific contagious virus of that disease is not present. After presenting a number of established facts bearing on this point, Dr. Biggs remarked that a wound or injury produced by the teeth of a non-rabid dog, one the saliva of which does not contain the living organism, whatever may be its nature, which is its essential cause, can no more bring about the specific disease which we call rabies than can the wound made by a sterilized knife.

As to the nature or character of this *contagium vivum*, we have at present no absolute knowledge, excepting that it must be a living matter capable of reproduction and multiplication when transferred to the living organism, and there producing a specific disease manifested by varying symptoms in the different species of animals affected; of the presence or virulence of which we can only know by the results produced when introduced into the blood of previously healthy animals. That it is exceedingly minute is shown by the difficulty experienced in its demonstration, and that it is a microörganism belonging to the Schizomycetes is rendered probable by the similarity observed to other known pathogenic microorganisms, as regards the mode of its transmission and development.

Having mentioned that Dr. Fol, of Geneva, had recently claimed to have discovered the specific microorganism, to have demonstrated it in the neuroglia of

the central nervous system, to have succeeded in cultivating it in appropriate culture media, and to have produced rabies in rabbits by inoculations with pure cultures of this germ, Dr. Biggs quoted *in extenso* this investigator's description of his methods of procedure as given in his communication on the subject to the French Academy. He then went on to say that the claims of Fol are not favorably regarded in Pasteur's laboratory, on the grounds, first, that the methods which he describes and used for the cultivation of the germ have been repeatedly employed by M. Roux, Pasteur's first assistant, without any result; second, that he describes the germ found by him as an aërobic, while from the nature of the rabies, and the presence of the *contagium vivum* in the nervous system, it seems far more probable that it is an anaërobic or facultative anaërobic germ; and, third, because he has produced rabies in rabbits, in which the disease manifests itself by no characteristic symptoms, as is the case with dogs, and in which rabies may be easily confounded with the various forms of septicæmia. If, then, we accept the only rational theory as to the etiology of rabies, the microbic nature of the cause, although a supposition that has not yet been proven excepting as we reason from analogy, and acknowledge the impossibility of the appearance of the disease except after inoculation with this living virus, the consideration of the methods for its prevention naturally follows.

Having referred to Pasteur's studies upon rabies up to the time of the meeting of the International Medical Congress in 1884, he remarked that some of the conclusions arrived at in his earlier work have not been confirmed either by his own later investigations or by those of other observers, and are in some respects opposed to the results recently reported. It must be admitted, also, he said, that unfortunately in his last communications he has not discussed the question so much in detail as could be desired, nor has he given definitely the number or character of the experiments upon which his conclusions and the general principles drawn from them are based. The failure to do this will render it impossible for any other investigator to repeat or confirm his experiments, and without such confirmation, from a thoroughly reliable source, there will of necessity be much reserve among scientific men about the acceptance of such important and far-reaching principles as are involved in his method for the prevention of rabies.

Dr. Biggs then gave a *résumé* of the former method of Pasteur for rendering dogs refractory to the disease, as presented in his communication to the French Academy, May 20, 1884. Having quoted the statements of Pasteur himself, that this process is dangerous in application, not sufficiently rapid, and not positive in its results, he proceeded to give a detailed account of Pasteur's present method, in regard to which the savant says, in the introduction to his latest communication: "After almost innumerable experiments, I obtained a preventive method, practical and prompt, of which sufficiently numerous and assured successes have already been obtained upon dogs to give me confidence in its general applicability to all animals and to man himself."

The efficacy of this method, he then went on to say, is proven by subjecting fifty dogs to these inoculations, with success in every case in rendering the animals refractory to rabies. After having arrived at these results, Pasteur felt justified, after consultation with Drs. Vulpian and Grancher, in subjecting to the process the boy Joseph Meister, who unexpectedly presented himself for treatment, July 6, 1885 In speaking of this case, Pasteur says: "I dare say that a smaller number of inoculations would have been sufficient, but it is easy to understand that the first trial was made with the observation of every possible precaution." In order to determine the virulence of the virus used, two rabbits were each day inoculated in the usual manner with the same virus as that used for the boy. These inoculations showed that the cords used on the 6th, 7th, 8th, 9th, and 10th of July were not virulent, since they did not produce rabies in the rabbits inoculated on those days. The cords used on July 11th, 12th, 14th, 15th, and 16th, however, were all virulent, and of a constantly increasing virulence. Rabies appeared after seven days of incubation in the rabbits inoculated with the cords of July 15th and 16th, after eight days in those of the 12th and 14th, and after fifteen days in those of July 11th. Notwithstanding that in the last inoculations virus was used which was far more virulent than that of rabid dogs which have contracted the disease in the ordinary way, still these inoculations were followed by no symptoms; and now that more than six months have elapsed since this boy was bitten, he yet remains perfectly well.

Since Pasteur's communication to the French Academy, October 26, 1885, his laboratory has been besieged by many persons, from all countries, who have been bitten by rabid dogs, and up to the time of Dr. Biggs's recent visit to Paris, 140 patients had been inoculated. Referring to the one case in which death from hydrophobia resulted shortly after the inoculations were completed, he said that, in explanation of the failure to prevent the appearance of the disease in this instance, Pasteur asserted that the period of incubation, as transmitted from the rabid dog, had elapsed before immunity had been conferred by the inoculations (thirty-six days having intervened between the bite and the commencement of treatment), and this explanation certainly seems reasonable when we remember that the period of incubation of rabies in the human subject, although usually more than thirty-six days, is not infrequently less than this time.

An interesting and serious question came up in connection with this death, viz., whether the disease might not have been the result of the inoculations rather than of the dog-bite, and a solution of this question was obtained in the following way: The virus of a rabid dog, when transferred to a rabbit by inoculation underneath the dura mater, after trephining, produces rabies, on an average, in fifteen days; while the most virulent cords used in the inoculations produce rabies with the greatest uniformity in rabbits in seven days, and in dogs in from eight to ten days. Pasteur asserted that if rabbits were inoculated in the usual manner with material from the brain or spinal cord of this child, if the disease in the child were produced by the inoculation, the rabbits would die of rabies, which declared itself after a period of incubation of seven days; but if the disease in the child was due to the inoculation made by the bite of the rabid dog, then rabies in the animals would not make its appearance until about the fifteenth day.

Accordingly, rabbits were inoculated from the child's brain removed at the autopsy, and it was found that they died with the usual symptoms of rabies, which appeared on or about the fifteenth day. The result of this experiment is apparently satisfactory; but there may, perhaps, be a source of error in the possibility of the periods of incubation of the respective virus being altered by their passage through the human subject.

Having referred to the importance, in connection with the conclusions to be drawn from the results of Pasteur's inoculations, of determining whether the dogs biting the various persons treated really had genuine rabies, he mentioned that in the case of the four Newark boys, not one of a number of dogs bitten by the dog which bit the children, nor either of the two boys which remained at home, had up to the present time exhibited any symptoms of rabies.

Having discussed the period of incubation of rabies in man and in animals, Dr. Biggs said that as to the interpretation of the prophylaxis against rabies, Pasteur states that the alteration in the virulence of the rabic cords by the process of desiccation, is explained on the supposition that the continuous contact of the dry air produces a gradual diminution in the intensity of the virulence of the cords, until it finally becomes extinct; that the prophylactic method in its application depends for its efficiency upon the employment at first of a virus without appreciable activity, followed by a weak virus, and then by a more and more virulent form; that the diminution of the virulence of the cords is due to an impoverishment in quantity of the virus contained in the cords, and not to an impoverishment in virulence. Consequently, in the inoculations the virus used is always identical as regards its virulence, and is variable only in respect to the quantity employed; so that the refractory condition to rabies follows from the employment of very small, but constantly increasing, quantities of virulent material.

This interpretation of the method of action of the virus is the more interesting, as a new and quite different principle is involved from that obtaining in the vaccine for smallpox, or the vaccines devised by Pasteur for the prevention of anthrax, chicken cholera, and typhus in pigs. In smallpox we have a virus modified in character and virulence by its passage through another species of animal; in anthrax, chicken cholera, and typhus in pigs we have a virus modified in respect to its virulence by the conditions of temperature to which it has been subjected during its developmental growth; and, finally, in rabies we have a prophylactic method dependent upon the employment of a virus always constant as regards its virulence, but used in very small and constantly increasing quantities.

Apparently, then, already there have been three distinct methods discovered for the preparation of preventive vaccines for the different forms of contagious disease. The theoretical principle has also been established by the researches of Pasteur, and more recently of Burdon-Sanderson, of the possibility of depriving cultures of pathogenic microörganisms of their virulence in a constant and persistent degree, without in any other respect affecting their morphological character. Taken in connection, these methods for preventive vaccinations present almost unlimited possibilities in preventive medicine, and possess a significance the importance and far-reaching nature of which can scarcely ever be comprehended.

Dr. Biggs said that in regard to the possibility of transmission of the disease by animals or human beings subjected to these inoculations, to other animals or human beings during the process of inoculation, or at any period after this time, Pasteur states that he has made no experiments or observations. As to the duration of the refractory condition to rabies after the series of inoculations, Pasteur believes this period to be not less than one year, and probably considerably longer than this; but no careful data upon this point are at present at hand.

Dr. Biggs then proceeded to discuss the conclusions which are to be drawn as to the accuracy of Pasteur's observations upon rabies and the efficacy of his method for its prevention. As to the first human subject inoculated, the boy Joseph Meister, he could not but entertain the opinion that the dog which bit him was not affected with genuine rabies. It was certainly very unlike the ordinary behavior of rabid animals to fall upon a person with such ferocity and persistency as must have been the case in this instance, where the lad was bitten in no less than fourteen different places. Again, the autopsy of the animal did not afford sufficiently satisfactory proof of the existence of rabies.

But however this might be, he thought far too much importance had been attached to this case, and it seemed to him that the strongest evidence of the efficacy of Pasteur's method for the prevention of rabies rests, not upon any results thus far obtained in the inoculation of human beings, but upon the results of his experiments upon dogs. If he has been able not only to render fifty dogs refractory to rabies, without a single failure, but also has succeeded in preventing the development of the disease in a large number of dogs after they had been bitten—both of which he asserts positively he has accomplished—then the question as to the prevention of the disease in human beings is only as to the method of application. Dogs are far more susceptible and liable to the malady than human beings, and the character of the disease being evidently the same in both man and dogs, if dogs can be brought into a refractory state to the disease, certainly it is not assuming too much to conclude that the same is true of the human being.

Dr. Biggs concluded in these words: "But, throwing aside the evidence which we have now at hand, as to the efficacy of Pasteur's method—and I think it must be said that it is not altogether satisfactory in character—let us consider the probability of the correctness of these last observations from the light thrown upon the subject by his former work. Does it seem probable that the man who, in the earliest infancy of bacteriology, disclosed the nature and cause of fermentation, and established our knowledge of it on a firm foundation in the face of much opposition and scepticism, the man who disproved the theory of spontaneous generation, and laid the foundations upon which rests our whole system of antiseptic surgery, who disclosed the nature of the plague in silkworms in France, and devised the methods for its prevention, who discovered the principles underlying the method of protective vaccination in the diseases of animals, and has prepared the only practicable vaccines; does it seem probable that such a man has given nearly six years of continuous study to the consideration

of rabies without achieving some substantial results? Or does it seem probable that he has been dealing all these years with some form of septicæmia, as has been suggested; laboring under the delusion in the meanwhile that it was rabies? This I cannot believe; and if it is not true, then Pasteur's conclusions must be in the main correct, for certainly no one will question his honesty. Every great discovery in science has been met with scepticism, opposition, and ridicule. . . . . Pasteur's prophylactic method rests purely on empirical grounds, and can only be fairly judged by the practical results obtained by its use. So far as we know at present, these have sustained the claims of its learned discoverer, and until they are refuted by further observations, we believe it is unjust to characterize the work of Pasteur, as has been recently done, as being founded 'on untrustworthy experiments and unsound reasoning, deserving to be rejected and condemned in the interests of humanity as well as science.' On the other hand, if future observations confirm the results that now seem to be at least probable, this discovery, added to his other achievements, will rank Pasteur as one of the greatest benefactors to his race that this generation has produced, and, from a scientific standpoint, will be considered one of the grandest triumphs of the century."

DR. A. FLINT, JR., said that it was proper to put the facts alleged by Pasteur, to the same tests as any new discoveries in physiology are required to be subjected to. It was not without precedent that this disease had been studied in the way that it has. From the fact that a prominent symptom in most cases of rabies is a spasm of the muscles of deglutition, especially excited by the sight of liquids, the renowned experimenter Magendie had attempted to cure a case of the disease in the Hôtel Dieu by intravenous injections of water; and it is hardly necessary to add that the attempt was a complete failure. Although this affection, on account of this symptom, is commonly known as hydrophobia, its true name is rabies, and this procedure on the part of Magendie does not seem like a philosophical method of treating the disease.

More recently, woorara poison, which has proved such a valuable agent in many physiological experiments, has been tried, by more philosophical methods, in the treatment of rabies. It is true that this also has been directed especially against a symptom; but it has also been employed for the purpose of counteracting a general pathological condition. A number of years ago, Offenberg reported a case of the disease cured; in 1850, a case of spontaneous cure was observed by a veterinary surgeon in Lyons; and in 1864, Décroix met with quite a number, all in dogs. A case of spontaneous cure has also been reported in the human subject. But all these alleged recoveries are clouded by one possibility, that of an error in diagnosis.

But Pasteur's method is one of prevention, as he does not propose to treat the disease after it has actually broken out in the system. According to the older ideas, rabies was propagated only by means of the saliva of certain animals, notably dogs and cats; and the saliva of the wolf has been regarded as of peculiar virulence. For a long time it was denied that any other fluid, or part of an animal suffering from the disease, was virulent; and it was also held, that the saliva of the herbivora and of the human subject were incapable of inoculating with rabies. In his preventive inoculations, Pasteur long since abandoned the use of saliva, and resorted to a method which is entirely artificial, viz., the injection of virus under the dura mater of rabbits, after trephining of the skull, in order to produce the disease in these animals, the spinal cords of which he uses in inoculating human beings.

It, therefore, becomes a vital question to determine whether these rabbits are actually affected with rabies or not, and Dr. Flint said that he did not know whether or not any one had ever given a precise description of this disease as it appears in rabbits. Pasteur states that the rabbits are rabid; and we are called upon to accept his dictum, without any evidence whatever to support it. He had himself, in connection with various physiological investigations, experimented upon a large number of rabbits, and he knew that their delicate nervous organizations are very seriously affected by operations much less serious than trephining. He believed, therefore, that before we could accept the statements of Pasteur as facts, it is necessary that they should be corroborated by such control experiments (such as the injection of bouillon without spinal marrow, etc.) as are demanded of any physiologist who professes to have discovered facts which were previously unrecognized. But if by any such means as those proposed by Pasteur a human being can be prevented from having rabies after exposure to the risk of the disease, it, of course, makes no difference whether the rabbits used in the process have rabies or not. This is the practical point; but when we come to a theoretical consideration of the matter, the condition of the rabbits is a circumstance of great importance. If investigators, even as illustrious as Pasteur, such as Magendie and Claude Bernard, for instance, had attempted to introduce any new points into physiological science which are not better supported by corroborative evidence than Pasteur's alleged discoveries, their statements would not have been accepted.

With regard to dogs, Dr. Flint inquired whether there was a single authenticated case of a dog contracting genuine rabies by inoculation from Pasteur's rabid rabbits. For such an alleged fact we have only Pasteur's own statements to depend on. Moreover, the dog that bit Joseph Meister did not act as rabid dogs ordinarily do, the animals being rendered insane by the disease. Again, a man bit by a rabid dog has about three chances out of four of not having rabies. In a large proportion of instances the bite is made through the clothing, and we might almost as well expect a vaccination to take which had been made in a similar way as to suppose that an individual would have hydrophobia under such circumstances.

Now, under our present knowledge of this subject, shall a human being be subjected to the possibility of inoculation with a poison which gives rise to one of the most frightful diseases known to man? The case of the little girl who died after inoculation by Pasteur, shows one of two things. Either that this period had elapsed between the bite of the rabid dog and the commencement of the preventive treatment, or else the disease was actually produced by the inoculations. Dr. Flint said that it is not absolutely certain that any dog had ever been rendered refractory to rabies by Pasteur, and that it is a necessary step in the application of the method to human beings to prove that

dogs which had actually been bitten by a rabid dog had been rendered refractory to the disease. When a dog becomes mad he does not first have his skull trephined, and the same is true of men. It is pertinent to inquire, therefore, whether dogs and persons rendered "refractory" by the Pasteur method are in reality refractory to rabies when conveyed into the system in the ordinary way. This question, he thought, had not as yet been answered in a sufficiently definite and satisfactory way. It was a curious fact that no phenomenon whatever was observed in the system while the process of inoculation was being carried on.

Dr. Flint then went on to say that the science of medicine had never received more glory than by the discovery of vaccination, by which more lives had probably been saved than by any other in the history of medicine. Not long since he had had occasion to go over the investigations of Jenner, as described in his published writings, and he had been more profoundly impressed than ever with the accuracy and logical sequence of his researches in the development of his great achievement. This scientific accuracy has not appeared in anything that has as yet been published by Pasteur, or under his authority. It is only his splendid and well-deserved reputation, as far as can be judged at present, which preserves him from the charge of asserting claims which he cannot substantiate on a scientific basis. If the Newark children are to be taken as samples of the 325 cases which he has just announced to the Academy of Sciences that he has successfully inoculated, the percentage of real successes in this number must be extremely small, since it has now been substantially proven that the dog that bit these children was not mad, by the fact that not one of seven dogs which were also bitten by the same animal, and which have been confined and carefully watched, has exhibited any indication of rabies after the expiration of more than ninety days.

DR. E. G. JANEWAY said that last summer, when he was in Paris, he was sufficiently interested to visit Pasteur's laboratory, although this was before his prophylactic process had been applied in the case of a human subject. He was cordially offered the opportunity of inspecting the method of inoculation, but not of the preparation of the virus used for the purpose. While there, he asked himself this question, which seemed to him to be the keynote of the whole matter: Have these dogs been rendered refractory to hydrophobia as conveyed in the ordinary way? This is the point of vital importance, and he said that if they *are* rendered thus refractory, he could see no objection to carrying out the same plan of inoculation in the human subject in any case where an individual has been exposed to the risk of contracting the disease.

As to the spinal marrow being employed as the agent for transmitting the virus, it seemed to him entirely appropriate. The virus which is lodged in the wound made by the bite of a rabid dog and remains there for a time, is undoubtedly composed of living matter. Thence it is diffused throughout the system. While it is present in the saliva, therefore, the manifestations of the disease show that the germ is also in the spinal marrow and the medulla oblongata, or, if this is not the case, that it circulates as a specific poison in the blood and acts as an irritant upon these nervous centres. In other analogous diseases we find after death the germs of the affection at or near the points of inflammation, and, therefore, it seemed altogether appropriate to employ these parts for the purpose of inoculation.

Whether the time has really come to subject human beings to these inoculations is perhaps open to question; but in any case where an individual has been bitten by a dog known to be mad, there would seem to be no objection in adopting Pasteur's method, which has, at all events, proved innocuous in more than three hundred cases. From the statements of Dr. Biggs and others, there seems to be no reason for doubting that dogs have really been rendered refractory to the disease by it.

As to the case of the Newark children, it is questionable whether the dogs bitten by the same animal as the boys, were kept under observation for a sufficiently long period. In Berlin under similar circumstances, dogs have been confined for six months, instead of three. Dr. Janeway thought it unnecessary to adopt the Pasteur process for the purpose of rendering dogs generally refractory to rabies, as vaccination is used among human beings to prevent them from having smallpox. Hydrophobia could be more satisfactorily prevented, he believed, by the rigid enforcement at all times of the law requiring dogs to be muzzled. Under such a provision in Berlin, not a case of the disease occurred for five years. Dr. Janeway stated, in reply to a question by Dr. Jacob Hartmann, that the period of incubation in hydrophobia is indefinite, but usually less than three months, and rarely or never more than a year.

DR. HARTMANN mentioned that he had met with a case in St. Louis in which the period of incubation, so far as could be judged, was but little less than five years.

DR. BIGGS remarked that the answer to most of the questions which had been raised lay in the proof of the genuine nature of the disease with which Pasteur has been working. This is a difficult matter to determine from an independent point of view. When in Paris, however, he saw a number of cases of dogs with all the typical symptoms of rabies developed in the ordinary way, as these are described in the books. Although without any previous personal experience with the disease, he would not hesitate to make the diagnosis of rabies in them. It is an indisputable fact that Pasteur has for years been experimenting with a disease which almost invariably runs the same course and produces the same symptoms; the period of incubation in rabbits being always about fifteen days. If this affection is septicæmia, as has been claimed by some critics, it must be an entirely new form of the trouble. We know of no variety of septicæmia which has a period of incubation in rabbits of fifteen days, and after cultivation, of seven days; while in dogs it is longer. Again, we know of no other disease except rabies which produces the symptoms noted in these cases, and which always results in death. In dogs the period of incubation of septicæmia, it may be stated, is about eight or nine days.

Dr. Flint had suggested that in connection with the inoculations, control experiments should be made, such as the injection of bouillon without any portions of spinal marrow being added, etc.; but while this particular procedure has not been tried, so far as he was aware, it is a fact that these inoculations have been made subcutaneously and into the veins, instead of under the

dura mater after trephining, and the only difference that has been noted in the result has been that the period of incubation is longer under these circumstances. The reason why Pasteur adopted the method which he now employs was because he found after many experiments that with it the period of incubation is shorter, and the process more certain, than when any other is used.

As to the manifestations of rabies in rabbits, Pasteur distinctly declares that the disease has no definite manifestation in these animals. In them it is analogous to many forms of septicæmia; and it was on this account that he (Pasteur) was unwilling to accept the results of Fol's investigations, which were practically based on the pathological conditions observed in rabbits after experiments; therefore, the only way to test the true nature of the disease resulting from inoculation, is to inoculate dogs with the virus; and in them it manifests itself by symptoms which are believed to be unmistakable.

As to the protection against the disease of dogs which have been bitten by other rabid dogs, Pasteur asserts positively that the most complete protection has been afforded in numerous instances. These animals were placed in cages together with dogs which were indisputably rabid, and having been bitten by the latter, were afterward subjected to the prophylactic inoculations; and in not a single instance has rabies subsequently resulted in them. These experiments have been repeatedly tried under the supervision of the official commission appointed to investigate the matter; and this evidence would seem to be of the greatest possible importance in establishing Pasteur's claim.

MONTREAL MEDICO-CHIRURGICAL SOCIETY.

Stated Meeting, March 5, 1886.

THE SECOND VICE-PRESIDENT, GEORGE WILKINS, M.D., IN THE CHAIR.

GUNSHOT WOUND OF FRONTAL LOBES OF BRAIN; SURVIVAL OF PATIENT FOR EIGHT DAYS.

DR. WYATT JOHNSTON exhibited the brain of a man aged forty-three, who had shot himself because he was told he was suffering from phthisis. The weapon used was a revolver, carrying a No. 32 ball. The ball entered the left temporal region, one and a half inches above the zygoma, and half an inch behind the external angular process of the frontal lobe. The bullet pierced the dura mater, and entered the posterior part of the third left frontal convolution, thence through the left hemisphere and falx cerebri, and entered the right hemisphere at the posterior part of the first right frontal convolution, where it pierced the dura mater. From this point there was a superficial furrow, having a downward and backward direction. The bullet, slightly flattened, was found in the posterior inferior part of the right ascending frontal convolution. The track of the bullet showed extensive hemorrhagic softening. There was also extensive extravasation of blood between the membranes; the ventricles were uninjured. On examining the chest, a double acute tubercular pleurisy was found, and hypostatic pneumonia. The patient died eight days after the accident, and had never spoken, but he was conscious, and apparently understood questions asked him. There was no complete paralysis, but there were occasional slow movements of right arm, and the left leg was kept crossed over the right; no tremor or spasm of any kind.

MULTILOCULAR OVARIAN CYSTOMA.

DR. WM. GARDNER exhibited an ovarian tumor, and gave a brief account of the case. The woman, æt. forty-eight, married, but sterile, consulted him six years ago for a moderately large cystic tumor, with solid nodules in the pelvis. Menstruation was increased. She was advised against operation, but saw another surgeon, who explored through an abdominal incision, but apparently did not otherwise interfere, as she appeared some time afterward unchanged in her condition, except for the scar and a ventral hernia. She was then lost sight of till two months ago, when she was admitted, under his care, into the Montreal General Hospital. She stated that, a few months after the exploratory incision, she began to enlarge rapidly, and pressure symptoms became so distressing that her attending surgeon tapped her many times. Four months previous to admission the tumor ceased to enlarge.

The lower part of the abdominal walls and lower limbs were very œdematous; the whole abdomen, except the upper part, was elastic, indistinctly fluctuating, and dull on percussion; the hypochondriac and epigastric regions were tympanitic, but gave distinct wave fluctuation; menstruation had ceased eight months previously. Patient was eager for operation, although she was made fully to understand its serious character, and it was decided to give her the small chance which the operation offered.

On opening the abdomen the tumor was found to be universally adherent to parietes, intestines, bladder, and everything in the pelvis. In separating the adhesions, the intestines were torn several times, but promptly sutured. Above the tumor was an encysted collection of peritoneal fluid, with the intestines floating in it, under this lay a large, very thin, translucent cyst attached to the tumor. Hemorrhage, although not excessive, was severe enough, aided by the long and severe operation, to exhaust the patient, so that it soon became apparent that her chances were almost nil. The base of the tumor contained the uterus and a large mass of calcareous matter and myomatous nodules. It was included in a Tait's wire clamp, constricted, and then amputated. Bleeding being nearly arrested, the abdomen was closed, and a drainage tube inserted. The patient died half an hour after being put to bed. The tumor was a multilocular cystoma, the large cysts containing large masses of papilloma, nodules of which were also found on the parietes of the abdomen. The mass of calcareous matter measured three and a half by two inches.

DISEASE OF LUMBAR VERTEBRÆ WITH ACUTE PULMONARY TUBERCULOSIS.

DR. ROWELL exhibited the second, third, and fourth lumbar vertebræ, removed from a female patient who had died of acute pulmonary tuberculosis. The central parts of the body of each vertebra contained a small cavity filled with pus. The cavity in the second communicated with the vertebral canal. The lungs of the same patient, studded with tubercles, were also shown.

DR. ARMSTRONG said that the patient had been under

his care in the Woman's Hospital; she had severe lumbar pain, which was relieved by the application of a Sayre's jacket. However, her temperature keeping up, and chills and sweatings being of frequent occurrence, an incision was made and the lumbar vertebræ were examined, but no pus found. The patient died soon after, and the above described conditions of lungs and vertebræ were discovered.

Dr. Armstrong exhibited a pair of

CYSTIC OVARIES

he had removed from a young unmarried woman. One of the cysts was adherent throughout its whole extent; there was troublesome oozing which was difficult to overcome; but the patient made an excellent recovery.

FRAGMENTS OF ROCK CRYSTAL REMOVED FROM THE CORNEA.

Dr. Buller exhibited three small fragments of rock crystal (the largest 1.5 mm. in length), which he had removed from the cornea of a marble-worker. They had been projected into the eye from the chisel of another workman. The patient came to Dr. Buller about an hour after the accident, and two small incised wounds of the cornea were found. These were parallel to one another, about 1 mm. apart, and nearly opposite to the lower margin of the pupil. After carefully examining the parts with focal illumination, he failed to find any foreign body, and prescribed a solution of atropine and a cold water compress. The patient returned for instructions from day to day, but despite the treatment the eye became more and more inflamed, so Dr. Buller explored the wound with a fine cataract needle. He at once felt the needle come in contact with gritty particles, thus giving unmistakable evidence of the presence of a foreign body, which was wholly invisible. On moving one of the particles some aqueous humor escaped, showing conclusively that the foreign body had partly penetrated into the anterior chamber, and from being invisible, would be extremely likely to be pushed into the anterior chamber during any attempt at extraction. Now the man had some time before lost the other eye, so that it was of the utmost importance to save this one. The eye was placed under the influence of cocaine and the blade of a broad needle was passed through the cornea into the anterior chamber, in such a way that the part containing the foreign bodies rested upon the flat surface of the needle. It was an easy matter then to remove the particles of rock crystal with a fine cutting needle, and without the slightest chance of their being pushed into the anterior chamber, a mishap which would have led to disastrous consequences. The eye, freed from the source of irritation, made a rapid and satisfactory recovery.

NEW YORK ACADEMY OF MEDICINE.

Stated Meeting, March 18, 1886.

The President, A. Jacobi, M.D., in the Chair.

THE RECENT DEATHS OF PROMINENT FELLOWS.

The Corresponding Secretary announced the death of ex-President Austin Flint, and of Drs. S. Oakley Vanderpoel and Gaspar Griswold, and moved that the Chair appoint a memorialist for each of the deceased. The motion being carried, the President stated that he would claim for himself the privilege of pronouncing a eulogy upon his illustrious predecessor, Dr. Flint, and that he would at a future meeting announce the memorialists for Drs. Vanderpoel and Griswold. He then said that he would appoint Dr. Stephen Smith to read a memoir of the late Dr. Alfred C. Post.

The discussion of the evening was on the subject of

GLYCOSURIA,

and was divided into two heads. The first was

THE SIGNIFICANCE OF SMALL QUANTITIES OF SUGAR IN THE URINE.

Dr. T. A. McBride said that in cases in which there is a small quantity of sugar in the urine, but no appreciable disease present, beside more or less disturbance of the nervous system, there is no question that great relief, and even possible cure, can be secured by appropriate treatment. In this class of cases, it is well known that sugar is frequently found in the urine in connection with pleurisy, phthisis, cardiac disease, cerebral hemorrhage, certain psychoses, and other affections.

It has been found that sugar, when existing in only small quantities in the urine, is not easily detected by the ordinary tests for this substance. Among the troubles which may be caused by its presence under these circumstances, however, may be mentioned: insomnia, so-called neurasthenia, paræsthesia, hemiparæsthesia, certain pareses, and even temporary hemiplegia. In all these conditions undoubtedly due to glycosuria, he had used the ordinary tests, and in many of them no indication of the presence of sugar was shown. To detect the sugar, it is necessary to filter the urine through blood charcoal, after which the charcoal is to be washed repeatedly with distilled water. After the second, third, or fourth washing, the sugar can be detected by Fehling's test. He had confirmed this test by means of the polariscope, and also by fermentation.

The amount of sugar found in these cases varies from a trace up to two and a half per cent., though as large a quantity as the latter is rare. In the treatment he uses diet, and as medicinal agents principally arsenic and Clemens's solution of bromide of arsenic. In conclusion, Dr. McBride said that he had to confess that he is at present somewhat at a loss how to determine what is diabetes and what is not. He saw so many cases of glycosuria without the thirst, emaciation, and other characteristic symptoms of true diabetes, that it is difficult to decide in the matter.

Dr. F. P. Kinnicutt said that Lauder Brunton found that after diluting the urine very considerably, and then testing in the ordinary way, he was often able to detect sugar in specimens in which, if the tests were made without the dilution, it was impossible to find a trace of it. Even in the case of normal urine, to which one or one and a half per cent. of sugar has been added, there often seems to be something present which permits the precipitation of the red oxide of copper.

Dr. Page said that there are three conditions in which sugar is found in the urine: first, in the urine of a healthy individual after eating sugar itself, or imbibing saccharine liquids; second, when found in great abundance, constituting the typical diabetes mellitus; and, third, when the quantity of sugar is small and intermittent. In both these latter conditions there is diabetes, but in the last-named the prognosis is much more favor-

able than in the other. Niemeyer mentions that diabetes is much more prevalent in men than in women, the proportion of cases being three to one; and while it generally occurs in men between the ages of thirty and forty, in women it is more often found at an earlier period of life. This, however, has not been his own experience, as he has found it more common in women than in men, and generally after the age of fifty years. In such cases it is usually intermittent, and not infrequently it has been the irritation of the vulva caused by the saccharine urine which has led him to make the examination for sugar.

In regard to the treatment, he said that he had no faith in any medicinal agent whatever. Opium may be of service at night in securing rest and preventing the frequent micturition which is often so annoying a symptom, but he did not believe that it had any curative power. He had heard Prof. Alonzo Clark express the same lack of faith in drugs, and when at Carlsbad last summer he had found that the physicians there who make a specialty of this disease, depend almost entirely upon diet and the waters of the springs. One great source of their success, he thought, was that at a place like Carlsbad patients could be kept much better under control than at their own homes, so that they would be willing to confine themselves scrupulously to the restricted diet imposed. When they went away from the Springs he had no doubt that they become worse again from imprudence in eating.

DR. GEORGE B. FOWLER said that when working in the laboratory of Prof. Dalton, in 1877, he had repeatedly found sugar in normal urine after the ingestion of sweets. It had, for some time, been known that sugar could not be detected by the ordinary tests under certain circumstances, and Dr. Dalton was accustomed to filter the urine through animal charcoal before applying the tests. If we take normal urine and add enough honey to it to make a thick gum, no precipitation of red oxide of copper will take place on the application of Trommer's test in the ordinary way. If, however, we imitate the method of Fehling's test by employing an excess of test-fluid and only a few drops of the saccharine urine, the precipitate will at once occur. This modification of Trommer's test he has found of great practical value. If sweets are taken freely, especially on an empty stomach, glycosuria is very apt to be produced, and hence when an individual consults him in whose urine he finds sugar, but not a high specific gravity, and who does not present the ordinary symptoms of diabetes, he always inquires whether he has habitually used sweets or suffers from defective digestion. Patients in which such a condition is found, as a rule, recover quickly under proper diet.

DR. WILLIAM H. DRAPER remarked that he had ceased to attach much importance to the occasional occurrence of very small quantities of sugar in the urine, for the reason explained by Dr. Fowler. He has found it very often, particularly in the lithæmic state, in which there are seen the evidences of intoxication. When there are excessive amounts of urates and also crystalline uric acid in the urine, sugar is very likely to be found. All these circumstances are to be attributed, in his opinion, to defective metabolism, and the treatment which renders the urine normal in other respects will also remove the sugar. As Dr. McBride remarked, it is difficult to say where diabetes really commences. Sugar is not infrequently found in the urine of patients having not only imperfectly assimilated hydrocarbons, but also imperfectly assimilated nitrogenous food, and, therefore, sugar is often to be regarded simply as an indication of dyspepsia. In true diabetes mellitus sugar is formed from azotized food.

DR. FOWLER said that he had forgotten to state that the substance which interferes with Trommer's test is the ammonia in the urine, which redissolves the red oxide of copper as soon as it is formed.

DR. MCBRIDE said that uric acid will sometimes cause precipitation of oxide of copper. Sugar, when persistently present in small quantities in the urine, seems to indicate an excess of sugar in the blood, and it is the *persistent* presence of sugar which is important. It may be another kind of sugar, not derived from glycogen, but from the muscles. Ordinary sugar can be detected after dilution of the urine, as was mentioned; but this requires filtering through blood charcoal.

DR. DRAPER said that he did not think we could distinguish any difference in the cases of nervous disturbance in connection with lithæmia, whether sugar was present in the urine or not. Bence Jones, of London, has remarked that the "sour disease," gout, is very closely allied to the "sweet disease," diabetes mellitus. Long ago he pointed out the important fact that gout and diabetes very frequently exist in the same families and even in the same individual.

DR. MCBRIDE agreed with Dr. Draper; but he also claimed that sugar was the actual cause of nervous symptoms, just as uric acid and other agents might be.

DR. E. D. HUDSON, JR., called attention to the importance of shock in the production of diabetes. Sugar has been found in connection with whooping-cough, the presence of enlarged bronchial glands, spasmodic asthma, and convulsions; and we are therefore led to conclude that it is the disturbance of the pneumogastric which affects the glycogenic function of the central nervous system.

THE PRESIDENT remarked that in a great many persons, at times, sugar is found in the urine in small quantities which can be detected by the ordinary tests. As a rule, such patients are beyond middle life. He said that when he was a student he was taught that diabetes was a very rare disease, and that it was always fatal. It is true that the cases of diabetes in which the specific gravity of the urine ranges from 1.040 to 1.060 are very rare; but cases in which it ranges from 1.017 to 1.035 are very frequent, and they are by no means always of a mild character. Still, quite a large number of such patients live for a long time, and some get entirely well. A considerable proportion of these cases are in gouty individuals. When their general health is good, very little sugar is to be found in the urine; but when they begin to fatten up and take little exercise the quantity of sugar may be sufficient to produce pruritus vulvæ in the case of females.

When such patients contract other diseases, however, and especially pulmonary affections, they are in the greatest possible danger; and, as a rule, they will not live through an attack of pneumonia. Even though there may have been no signs at all in the urine for months or years before, if they get pneumonia, the most pronounced glycosuria is apt to become suddenly de-

veloped. Such a case was that of a physician, forty-two years of age, which he mentioned. He had formerly had diabetes, and was an expert in urinary examinations, but for six years his urine had been absolutely free from sugar, when he was taken ill with pneumonia. For two days he did well; but he was then seized with intense thirst, and suspecting that there was a return of his old trouble, he asked to have his urine tested for sugar. This was accordingly done, and sugar was found in large quantities. As soon as he was informed of the result, he remarked, "Now I will go," and two days afterward he was dead. Dr. Jacobi said that, in his experience, every such case was doomed.

He then went on to speak of four brothers, whose ages ranged from fifty-seven to thirty-nine or forty, all of whom are or have been the subjects of diabetes. The first was taken in England about ten years ago. He never was willing to observe any care in his diet; the affection has progressed, and he is now the subject of pulmonary disease, so that it is not difficult to see that his days are numbered. The second brother, on the contrary, used extreme care in his diet, and paid general attention to his health, and there has not been a trace of sugar in his urine for four years. In the case of the third brother there is an occasional return of glycosuria after excesses in diet; and the fourth and youngest brother is now also diabetic. This history shows that in a large number of cases the presence of sugar in the urine indicates defective assimilation. If this condition is not treated, it may result in persistent diabetes, and finally terminate in pulmonary disease. He would say, therefore, that sugar in small quantities does not signify much so long as a general good state of health is maintained; but it may be the source of great danger when other diseases set in.

Dr. Frederick A. Burrall then spoke on

THE TREATMENT OF DIABETES

and referred to the dietetic, hygienic, and medicinal factors. In speaking of the first, he said that while in the earlier stages of the disease the food containing saccharine and starchy matter is the source of the sugar in the urine, in advanced cases it is also derived from nitrogenous food and the tissues themselves. Although there is some dispute on this point, he thought that pure milk is probably good in diabetes; it has been said that the lactic acid is not converted into glucose. Glycerine had been recommended by some as a substitute for sugar, but in his own experience he had found that this increased the amount of sugar in the urine. The good effects of such agents as the alkalies may be due to the gouty diathesis in connection with diabetes. Loomis speaks well of skim milk as an exclusive diet, if the patient can be induced to live on it, and Tyson considers it better than any medicinal agent; but no exclusive method has been found entirely satisfactory.

Of medicinal agents which have been used by various authorities, there is a very long list. Of those which have seemed to prove the most valuable he mentioned codeia, which has been given in quantities of from fifteen to forty-seven grains daily; ergot, in doses of half a drachm of the fluid extract, increased to a drachm; lactic acid, of which Casstain gave from seventy-five to one hundred grains a day; Clemens's bromide of arsenic solution. While all these agents appear to have proved of more or less service in connection with a restricted diet, none of them has been known to have any effect without this.

Dr. Cauldwell said that his remarks would be confined entirely to the so-called specific, jambol. About three months ago he received a letter from London from a former student, in which he said this agent is now accepted in the East Indies as a cure for diabetes. He had tested it in healthy adults, and it had not produced any constant physiological effects. He had also prescribed it in four cases of well-marked diabetes. In all the patients, before taking the drug, the daily quantity of urine passed exceeded one hundred ounces, and in all the specific gravity of the urine was above 1.030. Sugar was also abundant, and all the ordinary symptoms of diabetes were present.

All the patients were treated alike, and were kept on anti-diabetic diet, with a moderate amount of toasted bread. Five grains of the powdered seed of jambol were given three times a day. In Case I., the beneficial effect was much pronounced. In two months the patient gained twelve pounds in weight, and the sugar entirely disappeared from the urine. It has remained absent for the past month. In Case II., the remedy was given for four weeks without any apparent effect. In Case III., a gradual improvement has taken place. The daily quantity of urine passed is reduced to 82 ounces, and the specific gravity to 1.030; but sugar is still abundant. In Case IV., after five weeks of treatment, the daily quantity of urine was reduced to 50 ounces, and the specific gravity to 1.028. The patient has also gained ten pounds in weight.

In addition to these cases, Dr. Cauldwell said that through the courtesy of Dr. Samuel Alexander, he was enabled to report two others, which had been under the care of Drs. Keyes and Alexander. In the first of these the improvement was very satisfactory; but in the second there was no improvement whatever.

In four cases out of six, therefore, the use of jambol had been followed by improvement, while in two it had proved a failure. In other words, in two-thirds of this small number of cases, it had seemed beneficial, and in one-third not. He regretted that Dr. Weber was not present, as he understood that he had used this agent in a larger number of cases than himself.

Dr. Draper remarked that, excluding the dietetic treatment, it may be truly said that the treatment of this disease is as purely empirical as our knowledge of its pathology is speculative. There is no trustworthy testimony that drugs alone, without the more or less complete restrictions of saccharine and starchy food, are of any service; and while medicinal agents are undeniably useful as adjuncts, his experience led him to believe more and more that the dietetic and hygienic management constitute the essential factor in the successful treatment of this affection. The majority of cases of diabetes belong to the form of the disease known as benign. The severe cases, in which the sugar is derived not only from the hydrocarbons but from the nitrogenous food also, generally occur in persons who have received some severe shock or have been suffering from grave tissue changes in the system. In these, unfortunately, drugs are of little or no value.

Dr. Draper then said he would speak of but three agents which had proyed of especial service in his

hands: codeia, sulphide of calcium, and the alkaline carbonates. Opium, he thought, is a great boon to the diabetic. In regard to the sulphide of calcium, he said that his attention had first been called to it by Dr. Nathaniel Husted, formerly of New York, but now residing in Tarrytown on the Hudson. Dr. Husted, some years ago, while suffering from diabetes, employed sulphide of calcium in his own case for the relief of furuncles, with which he was at the time affected, and he was surprised to find that under its use the sugar disappeared from his urine. He remains well up to the present time, and is able to live on a simple mixed diet without causing any return of the glycosuria. He, himself, has found it a useful adjunct; prescribing it in one-fourth and one-half grain doses before meals. It is followed with good results in a large number of cases, especially in gouty patients, and he believes that it enables the subject of diabetes to indulge in a greater variety of diet than he could otherwise do.

As to the alkaline carbonates, he had found them very valuable. He believed that both gout and diabetes are not infrequently due to defective metabolism; and it is, therefore, a rational treatment under the circumstances to stimulate oxidation.

A gentleman present remarked that Dr. Husted still claimed to have excellent results with the sulphide of calcium, and that he had heard him say that when given for a sufficiently long period, he had never yet met with a case in which benefit was not derived from it. Dr. Husted considers Merck's sulphide of calcium the only reliable article in the market, and has never met with as good results from the product of any other manufacturer.

DR. M. G. DADIRRIAN said that in Constantinople and other points in the East, matozoon, or fermented milk food, is very largely used in the treatment of diabetes. In this preparation, which originated in Armenia many centuries ago, there is no sugar, the sugar being converted into lactic acid; and he believes that it is a very valuable adjuvant in this affection.

DR. ROBERT F. WEIR alluded to the subject of gangrene in connection with diabetes, and described three such cases which had recently come under his own observation. In looking up the literature of the matter, he had found extremely meagre information. In regard to amputation for this condition, many cases were reported of the small members, such as fingers and toes; but he had been able to find the record of but nine amputations of the thigh, and in only one of these did recovery take place. Under the circumstances he had naturally hesitated to perform this operation.

DR. S. VARICK said that there is one point in regard to the treatment of diabetes which had not received the attention in the present discussion which he thought its importance demanded. There are certain facts concerning the disease which he regarded as settled. In the first place, while glycogen is found in some of the solids and fluids of the body, and most commonly in the liver and muscles, it is a function of the liver to elaborate glycogen; and in diabetes this glycogenic function of the liver is increased. The question is, how to base our treatment on these facts. If it were in our power, we would, of course, check this glycogenic function; but, failing in this, our endeavor is to diminish the supply of material. It is important to follow the pointing of physiology as regards the muscles; and muscular exercise, both passive and active, is, therefore, of great importance in the treatment of diabetes. In this affection it is common to find the patient constantly subject to lassitude and indolence, and the physician should endeavor to overcome this by encouraging the diabetic to take exercise. Thus, he can make it a rule that his patient shall have so much bread after he has taken so much exercise. In the feeble cases massage is of very great value, and the point that he made was, that appropriate exercise is of much benefit as suitable diet.

DR. DRAPER remarked that enforced exercise is liable to be much abused. It is a great error in serious cases, he thought, to cause the patient to take too much exercise, and grave accidents not infrequently result from overfatigue.

DR. KINNICUTT mentioned, in this connection, the case of a patient who died from diabetic coma soon after arriving at the hospital; this being the result, as he believed, of the fatigue incident to a journey of some distance. In regard to amputations for gangrene associated with diabetes, he knew of a case, two weeks ago, in this city, in which the patient died of diabetic coma forty-eight hours after amputation of the thigh, for this condition.

NEWS ITEMS.

UNIVERSITY OF EDINBURGH. — The new chairs of Comparative Embryology and Natural Philosophy have been respectively filled by J. Brook and G. J. Romanes.

AMERICAN SURGICAL ASSOCIATION.—The annual meeting of the American Surgical Association will be held in Washington, April 28th, 29th, 30th, and May 1st. This will be an important meeting, and a full attendance of the Fellows is desired.

APPOINTMENT OF DR. STRATFORD.—The Trustees of the College of the City of New York have appointed William Stratford, M.D., Ph.D., to the chair of Professor of Natural History, Physiology, and Hygiene, made vacant by the death of the late Dr. John C. Draper.

PRIZES OF THE FRENCH ACADEMY OF MEDICINE.—The following prizes will be awarded in December, 1886: Hygiene of Infancy: Relation of Rachitis and Syphilis in Infancy, sixteen hundred francs. Prix St.-Lager: Fifteen hundred francs as a recompense for the experimentation which shall produce thyroid tumor in animals as a result of the ingestion of substances extracted from the water or earth of regions where goitre is endemic.

FRENCH SURGICAL CONGRESS.—The second session of the French Congress of Surgeons will be held this year in Paris from the 18th to the 22d of October.

The subjects proposed for general discussion, and to which the first four days are to be devoted, are:

1. Nature, pathogenesis, and treatment of tetanus.
2. Nephrotomy and nephrectomy.
3. Orthopædic resections.
4. Operative intervention in irreducible traumatic luxations.

DEATH OF PROFESSOR COURTY,—The death of Dr. Courty, Professor in the Surgical Clinic in the Montpellier Faculty, and one of the founders of the *Annales de Gynécologie et Obstetrique*, has just been announced.